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(54) Title: GENE DISCOVERY THROUGH COMPARISONS OF NETWORKS OF STRUCTURAL AND FUNCTIONAL RELATIONSHIPS AMONG KNOWN GENES AND PROTEINS (57) Abstract The present invention relates to methods for identifying novel genes comprising: (i) generating one or more specialized databases containing information on gene/protein structure, function and/or regulatory interactions; and (ii) searching the specialized databases for homology or for a particular motif and thereby identifying a putative novel gene of interest. The invention may further comprise performing simulation and hypothesis testing to identify or confirm that the putative gene is a novel gene of interest. The present invention also relates to natural language processing and extraction of relational information associated with genes and proteins that are found in genomics journal articles. To enable access to information in textual form, the natural language processing system of the present invention provides a method for extracting and structuring information found in the literature in a form appropriate for subsequent applications.		

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**GENE DISCOVERY THROUGH COMPARISONS OF NETWORKS
OF STRUCTURAL AND FUNCTIONAL RELATIONSHIPS
AMONG KNOWN GENES AND PROTEINS**

SPECIFICATION

5 The invention described herein was funded in part by a grant from the National Library of Medicine, namely, Grant Number's LM06274 and LM05627. The United States Government may have certain rights to the invention. The present specification contains a computer program listing which appears as a microfiche Appendix H.

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An appendix containing source code listing utilized in practicing an exemplary embodiment of the invention is included as part of the Specification.

1. INTRODUCTION

20 The present invention relates to methods for identifying novel genes comprising: (i) generating one or more specialized databases containing information on gene/protein structure, function and/or regulatory interactions; and (ii) searching the specialized databases for homology or for a particular motif and thereby identifying a putative novel gene of interest. The invention may further comprise performing simulation and hypothesis testing to identify or confirm that the putative gene is a novel gene of interest.

The present invention relates to natural language processing and extraction of relational information associated with genes and proteins that are found

in genomics journal articles. To enable access to information in textual form, the natural language processing system of the present invention provides a method for extracting and structuring information found in the literature in a form appropriate for subsequent applications. Specifically, the present invention provides for the
5 generation of specialized databases containing information on gene/protein structure, function and regulatory interactions based on the retrieval of such information from research articles and databases, and computer representation of such information in a manner that allows efficient access to the extracted information.

The invention further provides for the use of the specialized databases
10 for identifying novel genes based on detection of sequence similarities and domain/motif matches between genes/proteins, computation and interpretation of phylogenetic trees for multigene families, and analysis of homologous regulatory networks. The methods of the invention are based on the observation that functionally similar regulatory systems are generated during evolution by genetic duplication of
15 ancestral genes. Thus, a comparison of homologous/similar networks within the same organism and between different species will allow the identification of genes absent in one of the systems under comparison. In this way genes that contribute to the phenotype of a specific disease associated with a particular biological system under analysis may be identified.

20 2. BACKGROUND OF THE INVENTION

2.1. NATURAL LANGUAGE PROCESSING

Researchers working in molecular biology must constantly consider the information present in the literature relating to their regulatory systems of interest and the genes and proteins that operate within those systems. Unfortunately, to remain up-
25 to-date on the relevant literature, the researcher is required to perform laborious reading and manual integration of research articles, each of which may address a narrow subject. Therefore, technology that enables rapid retrieval of information from literature and manipulation of derived functional data should have a dramatic effect on the access of the researcher to important facts and ultimately should facilitate the
30 discovery of novel human genes.

Natural language processing is an automated system that provides for a complex of programs for automatic retrieval of information from text analysis and for the computer representation of that information in a form that allows efficient access and extraction of that information. MedLee (Medical Language Extraction and Encoding System) has recently been successfully used for processing different types of medical texts as described in co-pending United States Patent Application Serial Number 09/370,329, incorporated herein in its entirety by reference (see also, Friedman et al., 1994, J. Amer. Med. Inf. Assoc. 1:161-174; Hripcsak et al. 1995, Ann. Intern. Med. 122:681-688; Hripcsak et al., 1998, Meth. Inform. Med.; Jain et al., 1996, Proc. AMIA Annu. Fall Symp. 542-546; Knirsch et al., 1998). When tested, MedLEE was on average as successful in retrieving reports associated with specified clinical connections as twelve medical experts invited for evaluation of the system.

Another text analysis technique has recently been developed that combines finite-state machines with statistical machine learning approaches. These models extract detailed semantic information from texts (e.g., see Hatzivassiloglou 1996, In Klavens, J.L., and Resnick, P.S. (eds) *The Balancing Act: Combining Symbolic and Statistical Approaches to Language*, MIT Press, Cambridge, MA) when extensive prior knowledge about the domain is not available. The techniques have been subsequently applied to the tasks of (i) automatically identifying medical terms for the automated summarization of research articles reporting on clinical studies and (ii) sanitizing sensitive information in patient records so that they can be widely disseminated for research purposes.

A number of projects have also been developed as statistical information extraction tools that operate with limited or no prior knowledge about the application domain. These earlier efforts include XTRACT, a tool that recovers collocational restrictions between words that has been licensed to more than thirty sites worldwide (Smadja, F., 1993, J. Comp. Ling. 19:143-177), CHAMPOLLION, a system that retrieves bilingual mappings between words and phrases in parallel texts from different languages (Smadja, F. et al. 1996, J. Computational Linguistics 22:1-38), and a system that automatically aligns noisy, semi-parallel texts from different languages (Fung, P. and McKeown, K.R., 1997, Machine Translation 11:23-29).

2.2. IDENTIFICATION OF NOVEL GENES

A variety of different methods are currently utilized for the identification and characterization of novel genes. Perhaps the most widely used method for generating large quantities of sequence information is via high throughput nucleotide sequencing of random DNA fragments. A disadvantage associated with this gene discovery technique is that in most instances when genes are identified their function is unknown.

For identification of specific disease genes, positional cloning is currently the most widely used method. The positional cloning approach combines methods of formal genetics, physical mapping and mutation analysis and usually starts with a precise description of the disease phenotype and a tracing of the disease through families of affected individuals. Genetic linkage data obtained from the analysis of affected families frequently allows the determination of an approximate genomic localization of the candidate disease gene with a precision of several millions of nucleotides. Once localized, the genetically defined chromosomal region is then recovered from genomic libraries as a contiguous set of genomic fragments. Genes residing in the disease-related region are determined by analysis of transcripts that are transcribed from the genomic fragment. From this analysis an initial set of candidate genes for a particular disease are identified based on the presence of the gene product in the biological system affected by disease and a correlation between its expression pattern and the pattern of disease progression.

Important information for selection of candidate genes also comes from analysis of their homology with genes known to be part of the same or related biological system. Finally, the ultimate proof of association between a gene and a genetic disorder comes from mutational analysis of a gene in patients affected by the disorder and from demonstration of a statistical correlation between occurrence of mutation and the disease phenotype.

Although positional cloning is a powerful method for gene discovery, the experimental method is extremely tedious and expensive. Moreover, disease genes implicated in genetically complex disorders, *i.e.*, those controlled by multiple

loci, can hardly be found using this strategy because of the complications associated with multiple loci linkage analysis.

Specialized databases for homology searches have also been utilized in disease gene discovery projects. In recent years a number of efficient sequence comparison tools have been developed such as the BLAST (Basic Local Alignment Search Tool) family of programs designed for comparison of a single "search sequence" with a database (see Altschul et al., 1990, J. Mol. Biol. 215:403-410; Altschul et al., 1997, Nucleic Acids Res. 25:3389-3402), the family of Hidden Markov Model methods for comparison of a set of aligned sequences that usually represent a protein motif or domain with a database (e.g., Krogh et al., 1994, J. Mol. Biol. 235:1501-1531; Grundy et al., 1997, Biochem Biophys. Res. Commun. 231:760-6) and various other comparison tools (Wu et al., 1996, Comput. Appl. Biosci 12:109-118; Neuwald et al., 1995, Protein Sci. 4:1618-1632; Neuwald, 1997, Nucleic Acids Res. 25:1665-1677).

When used in disease gene discovery projects, homology searches can be enhanced by creating specialized databases that utilize statistical analysis for evaluating significance of sequence similarities in comparison of new sequences with a database of known sequence. Such databases are fine-tuned to the size of the database used (Altschul et al., 1990, J. Mol. Biol. 215:403-410; Altschul et al., 1997, Nucleic Acids Res. 25:3389-3402), so that the same level of homology between a search sequence and a database sequence can be determined to be highly significant if the search sequence is compared with a smaller database, or insignificant and thus undetectable, if the search sequence is compared with a larger database.

In alternatives to standard homology searches, in projects oriented towards gene discovery, researchers usually have some *a priori* knowledge about the set of genes/proteins that might display important similarity to the unknown new gene. Therefore, selecting an *a priori* defined set of genes/proteins for comparison with new experimental sequences is a feasible and useful strategy. This strategy was successfully applied to search for homologs of disease genes in yeast and nematode genomes by Mushegian et al. (1997, Proc. Natl. Acad. Sci USA 94:5831-5836).

Two homologous genes taken from different species that originate from the nearest common ancestor by speciation are referred to as orthologs, while any two genes that originate from a common ancestor via a series of events involving intragenomic duplications are called paralogs. Tatusov et al. (1994, Proc. Nat'l. Acad. Sci USA 91:12091-12095) describe comparisons of proteins encoded by the genomes of different phylogenetic lineages and elucidation of consistent patterns of sequence similarities permitting the delineation of clusters of orthologous groups (COGs). Each COG consists of individual orthologous genes or orthologous groups of paralogs from different phylogenetic lineages. Since orthologs typically have the same function, the classification of known genes and proteins into clusters of orthologous groups permits the assignment of a function to a newly discovered gene or protein by merely classifying it into a COG. Although Tatusov describes a method for assigning a function to a newly discovered gene, he does not describe a method for predicting the existence of undiscovered genes. In addition, Yuan, et al. attempted simultaneous reconstruction of a species tree and identification of paralogous groups of sequences and detection of orthologs in sequence databases (Yuan et al., 1998, *Bioinformatics* 143:285-289).

Other groups have aimed at capturing interactions among molecules through the use of programs designed to compare structures and functions of proteins (Kazic 1994, In: Molecular Modeling: From Virtual Tools to Real Problems, Kumosinski, T. and Liebman, M.N. (Eds.), American Chemical Society, Washington, D.C. pp. 486-494; Kazic, 1994, In: New Data Challenges in Our Information Age Glaesar, P.S. and Millward, M.T.L. (Eds.). Proceedings of the Thirteenth International CODATA Secretariat, Paris pp. C133-C140; Goto et al., 1997, Pac. Symp. Biocomput. p. 175-186; Bono et al., 1998, Genome Res. 8:203-210; Selkov et al., 1996, Nucleic Acids Res. 24:26-28). These projects are significantly different from the inventive methods described herein because they do not describe methods for deducing the existence of as yet unknown genes based on comparisons of regulatory pathways and gene structure between one or more species. The present invention provides a method for increasing the sensitivity of analysis methods through the generation of specialized databases.

3. SUMMARY OF THE INVENTION

In accordance with the present invention there is provided methods for identification of novel genes comprising (i) generating one or more specialized databases containing information on gene/protein structure, function and/or regulatory interactions; and (ii) searching the specialized databases for homology or for a particular motif and thereby identifying a putative novel gene of interest. The invention may further comprise performing simulation and hypothesis testing to identify or confirm that the putative gene is a novel gene of interest.

The invention is based, in part, on the observation that functionally similar regulatory systems are generated during evolution by genetic duplication of ancestral genes. Thus, by comparing phylogenetic trees or regulatory networks and identifying genes and/or proteins absent in one system under comparison, the existence of as yet unidentified genes and/or proteins can be predicted. To make meaningful comparisons of phylogenetic trees it is necessary to distinguish between orthologs and paralogs. The present invention provides a method useful for discriminating between orthologs and paralogs and inferring the existence of as yet unidentified genes and/or proteins.

The present invention relates to natural language processing and extraction of relational information associated with genes and proteins that are found in genomics journal articles. Specifically, the natural language processing system of the invention is used to parse the articles published in biological journals focusing on structure and interactions among genes and proteins followed by computer representation of such interactions.

In accordance with the present invention, specialized databases are developed that contain information on gene/protein structure and interactions based on information derived from preexisting databases and/or research articles including information on interactions among genes and proteins, their domain/motif structure and their subcellular and tissue expression/distribution patterns.

The invention relates to a sequence analysis program which utilizes the specialized database for comparison of a single sequence, processing the output into a sequence alignment, computing phylogenetic trees, and analyzing these trees to

predict undiscovered genes. This program also includes a set of tools for generating motif/domain models from multiple sequence alignments of known genes and for using these models for extraction of structurally and/or functionally homologous sequences from databases which contain raw sequence data.

5 The invention further provides for a simulation and hypothesis testing program which relies on the specialized databases of gene/protein interactions for identifying potentially undiscovered members of multigene families through comparisons of regulatory networks for different species and testing hypotheses with regard to regulatory cascades. A comparison of homologous regulatory networks
10 within the same organism and between different species of organisms will allow the identification of genes absent in one of the systems under comparison, thus providing a set of candidate genes. In this way, genes that contribute to the phenotype of a specific disease associated with a particular biological system under analysis may be identified, mapped and subjected to mutational analysis and functional studies.

15 4. BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a block diagram illustrating the three major programs of the method according to the present invention: (i) the generation of specialized databases based on information on gene/protein structure, function and regulatory interactions derived from research papers and databases; (ii) sequence analysis; and
20 (iii) simulation and hypothesis testing;

Figure 2 is a block diagram of an information extraction system in accordance with a preferred embodiment of the present invention;

Figure 3 is a diagram illustrating the object representation of molecules and relations between them;

25 Figure 4 shows a set of keywords defining proteins involved in apoptosis pathways, these keywords having been utilized for generating a specialized sequence database Apoptosis3, this list having been compiled manually for testing the concept of specialized databases;

Figure 5 shows a "species tree," which is a graph depicting the correct
30 order of speciation events leading to a set of present day species; a "gene tree," which

is a graph depicting a history of a few genes from the same species, where each species can be represented by multiple paralogous genes (because the set of known genes is incomplete for most genomes, and there are often multiple representations of the same gene family in the same genome, the gene tree can be drastically different from the corresponding species tree); and a “reconciled tree”, which is the gene tree that would be obtained if gene deletions were completely forbidden and all genes were known for all species under analysis;

Figure 6 shows the original tree of ALDH sequences, indicating sequence clusters where bacterial, plant, fungal and nematode orthologous genes are present, but a human ortholog was not yet known;

Figure 7 shows the same phylogenetic tree as in Figure 6 with an additional human protein, referred to as antiquitin which was discovered by the method of the invention;

Figure 8 is a schematic diagram illustrating functional network-based gene discovery in accordance with the present invention;

Figure 9A presents diagrams depicting the regulatory relationships among hypothetical proteins (denoted with Arabic numerals) of hypothetical species A and B. Proteins in different species denoted with the same numeral are considered orthologous. The diagrams show that regulatory relationships between a pair of proteins can be of three different kinds;

Figure 9B, 9C, and 9D are diagrams representing Boolean operations OR, AND, and XOR, on arcs of the two oriented graphs of Figure 9A, the same operations being applicable to the set of vertices of the two oriented graphs;

Figure 10 is a diagram representing a hypothetical example of defining homologous protein networks in two different species using protein motifs, the diagram showing only two hypothetical proteins (1 and 2) for species A and three hypothetical proteins (1, 3, and 4) for species B. Protein 1 in both species has motifs α and β , protein 2 has motifs δ , ϵ , and ζ , and proteins 3 and 4 have motifs δ and ζ , and ϵ , respectively. The motif analysis can indicate that proteins 3 and 4 in species B may collectively perform the same function as protein 2 in species A;

Figure 11A and 11B are diagrams respectively representing hypothetical examples of evaluating the impact of a "knockout" of hypothetical gene A on the expression of a hypothetical gene B. The effect of knock-out of gene A calculated by multiplication along the shortest pathway connecting genes A and B is inhibition of gene B, the resulting effect being zero if the orientation of only one arc in the same pathway is reversed;

Figure 12 is a flow chart representing the scheme of gene discovery analysis involving motif/domain analysis in accordance with the present invention; and

Figure 13 Identification of genes in *C. elegans* containing either POZ or kelch domains. The protein accession numbers are indicated adjacent to the different protein domains. The protein corresponding to accession number gi/1132541 contains a POZ domain, death domain, kinase domain and heat repeat.

Figure 14A. Two human sequences with the closest homology to the *C. elegans* sequence gi/1132541.

Figure 14B. Computed gene tree indicating that the identified human gene represents an ortholog of the *C. elegans* gene gi/1132541.

Figure 14C. Nucleotide sequence of the death domain gene.

Figure 14D. Deduced amino acid sequence of the death domain protein.

Figure 15. Identification of candidate gene implicated in the etiology of Chronic Lymphocytic Leukemia (CLL). Sequence homology between a CLL region open reading frame and mouse Rpt1 (sp/P15533/RPT1) is presented.

Figure 16A-B. Model of regulatory functions of Rpt1. Figure 16A indicates that in mouse T lymphocytes Rpt1 serves as a repressor of the gene for interleukin 2 receptor (IL-2R). Figure 16B demonstrates that when Rpt1 is knocked out, the regulatory effect is manifested as a block of the apoptotic pathway for T-lymphocytes resulting in accumulation of T-lymphocytes in blood.

Figure 17A. Two EST sequences identified by searching a protein dbEST using the mouse Mad3 protein as a query.

Figure 17B. Nucleotide sequence of the human Mad3 gene.

Figure 17C. Complete sequence of the human Mad3 protein. A search was conducted to identify overlapping sequences. The complete sequence of the gene was assembled and the amino acid sequence deduced. The translated human Mad3
5 sequence consists of 206 amino acid residues 81% of which are identical to the mouse Mad3 protein.

Figure 17D. Multiple alignment of the human Mad3 amino acid sequence with known Mad proteins.

Figure 18A. Phylogenetic tree indicating relationship between three
10 known mouse Mad genes and their two human homologs.

Figure 18B. Phylogenetic tree including new human Mad3 sequence. The phylogenetic tree indicates that the new human gene belongs to the family of Mad proteins and is an ortholog of mouse Mad3.

15 5. DETAILED DESCRIPTION OF THE INVENTION

The present invention provides methods for identification of novel genes comprising: (i) generating specialized databases containing information on gene/protein structure, function and regulatory interactions and, (ii) sequence analysis which includes homology searches and motif analysis thereby identifying a putative
20 novel gene of interest. The invention may further comprise performing simulation and hypothesis testing to identify or confirm that the putative gene is a novel gene of interest.

The specialized databases are constructed utilizing information concerning gene/protein structure or function derived from unpublished data, research
25 articles and/or existing databases. The specialized databases can be used to identify novel genes by: (i) searching for motif/domain combinations characteristic for a putative gene of interest; (ii) phylogenetic tree analysis of homologous genes for predicting the existence of yet undiscovered genes; (iii) comparing members of interactive gene/protein networks from different species for predicting the existence of
30 yet undiscovered genes; and (iv) testing a hypothesis with regard to known interactions of homologs from other species in regulatory pathways.

5.1. THE NATURAL LANGUAGE PROCESSING

The present invention relates to a natural language processing system that is designed to parse the electronic versions of articles published in journals that report on structural interactions among genes and proteins. The system provides a
5 method for extracting information on interactions among genes and proteins, their domain/motif structure, and/or their sub-cellular and tissue expression/distribution patterns, followed by computer representation of such information.

The general natural language-processing system of the invention is schematically depicted in Figure 2. The collection phase automatically collects
10 articles from appropriate literature, and selects articles that contain relevant information using Keyword search techniques. In the next phase, the preprocessor standardizes the selected articles so that they consist of tagged ASCII text where the tags delineate critical components of the article. The next phase, termed the extraction phase, retrieves and classifies biological entities, *i.e.*, as names of proteins, genes and
15 small molecules. In addition, the relationship extraction phase recovers structural relationships between the entities. This phase is followed by a phase which performs an analysis of the sequence of events.

The final phase of the system processes the output extracted from an article to remove redundancies, inconsistencies and to incorporate implicit
20 information before adding the extracted knowledge consisting of biological entities, their attributes, conditional constraints, and relationships between them, for subsequent use in analysis and hypothesis testing. The information extraction system as depicted in Figure 2, referred to herein as "GENIE," is designed for use as a general processor within the domain of genomics literature although the system may also be
25 used in other specialized domains. GENIE is an adaptation of MedLEE developed for the medical domain. GENIE uses the same source code as MedLEE but the Lexicons and grammar were adapted for genomics literature.

The information extraction system of the present invention is described below, by way of example, with reference to the genomics domain uses of GENIE. It
30 is written in Quintus Prolog and uses the Unix or Windows operating systems, as described in detail below.

A natural-language phrase included in text document is understood as a delimited string comprising natural-language terms or words. The string is computer readable as obtained, *e.g.*, from a pre-existing database, a keyboard input, optical scanning of typed or handwritten text, or processed voice input. The delimiter may be
5 a period, a semicolon, an end-of-message signal, a new-paragraph signal, or any other suitable symbol recognizable for this purpose. Within the phrase, the terms may be separated by another type of delimiter such as a blank or another suitable symbol.

As a result of phrase parsing, terms in a natural-language phrase are classified, (*e.g.*, as referring to a gene, a protein, or their interactions) and the
10 relationships between the interactions are established and represented in a standard form. For example, in the sentence "Rap inhibited fyn", the structured form would be:

[action,inactivate,[protein,rap],[protein,fyn]].

In such an example, the interaction is "inactivate", the agent is "Rap" and the target
15 is "fyn." More complex sentences consisting of nested relationships, such as "The activation of BAD was suppressed by the phosphorylation of JNK" can also be parsed and represented appropriately. The structured output form for this sentence would be:
[action,inactivate,[action,phosphorylate,x,[protein,jnk],[action,activate,x,[protein,bad]
]

20 In the first example, the primary interaction is "inactivate"; in the second example, an interaction "phosphorylate" is the agent where the protein "jnk" is its target (the agent of "phosphorylate" is not specified and thus is represented as "x"). In this example, the target of "inactivate" is also an interaction "activate" where the target is the protein "bad" and the agent is unknown.

25 While parsing is based on both syntactic and semantic grammatical patterns, the substances in a domain are normally only semantic categories such as "protein", "gene", and "small molecule." There are no corresponding syntactic categories needed for these substances because they are normally all nouns. However, each action can be categorized both semantically and syntactically. An action, which
30 is a semantic category, can generally occur syntactically as a verb "inactivate" or as a noun "inactivation." Therefore there are two sets of lexical entries for the actions:

syntactic and semantic. The syntactic lexicon for actions specifies the main syntactic category such as “v” for verb, “ving” for progressive form of verb, and “activation” for noun. The semantic entries for actions not only categorize the actions, but also specify features for each action. For example, one feature provides the number of arguments that are expected for the action, *i.e.*, some actions are associated with two arguments because they have an agent and a target as “inactivate”, and others just have an agent “mutate.” The lexicon of substances and structures appears as Appendix A; the syntactic lexicon for actions appears as Appendix B; and the semantic lexicon of actions appears as Appendix C.

A second feature specifies whether or not the arguments should be reversed when obtaining the target form. For example the arguments of “attributable to” should be reversed, *i.e.*, in “the phosphorylation of jnk is attributable to the activation of bad”, the underlying action is “cause” (from “attributable to”), the agent is the “activation of bad” and the target is “the phosphorylation of jnk”), whereas the arguments of “activates” is not(*i.e.* in “jnk activates bad” , the agent is “jnk” and the target is “bad”).

Figure 2 shows a preprocessor module of GENIE by which natural-language input text is received. The preprocessor thus performs lexical lookup to identify and categorize multi-word and single word phases within each sentence. The output of this component consists of a list of word elements where each element is associated with a word or multi-word phrase in the report. For example, assuming that the sentence “bad functions as a negative regulator of the activation of jnk” is at the beginning of the report, it would be represented as a list of elements where each element is a word or phrase. For example, element 1 is associated with “bad”, element 2 with the multi-word phrase “functions as a negative regulator of”, element 8 with “the”, and element 9 with “activation”. The remainder of the list of word positions would be associated with the remaining words in the report. Some of the phrases may not need lexical lookup because they already have been tagged by a previous component. Such a tagging system is described below in Section 5.2.

The second component of the GENIE system is the parser. It utilizes the grammar and categories assigned to the phrases of a sentence to recognize well-

formed syntactic and semantic patterns in the sentence and to generate structured output forms. The parser proceeds by starting at the beginning of the sentence element list and following the grammar rules. When a semantic or syntactic category is reached in the grammar, the lexical item corresponding to the next available
5 unmatched element is obtained and its corresponding lexical definition is checked to see whether or not it matches the grammar category. If it does match, the word or phrase is removed from the unmatched sentence list, and the parsing proceeds. If a match is not obtained, an alternative grammar rule is tried. If no analysis can be obtained, an error recovery procedure is followed so that a partial analysis is
10 attempted. The actual grammar used for GENIE appears as Appendix D.

The parser module of GENIE uses the lexicon, and a grammar module to generate target forms. Thus, in addition to parsing of complete phrases, subphrase parsing can be used to an advantage where highest accuracy is not required. In case a phrase cannot be parsed in its entirety, one or several attempts can be made to parse a
15 portion of the phrase for obtaining useful information in spite of a possible loss of information.

Conveniently, each module is software-implemented and stored in random-access memory of a suitable computer, *e.g.*, a work-station computer. The software can be in the form of executable object code, obtained, *e.g.*, by compiling
20 from source code. Source code interpretation is not precluded. Source code can be in the form of sequence-controlled instructions as in Fortran, Pascal or "C", for example. Alternatively, a rule-based system can be used such as Prolog, where suitable sequencing is chosen by the system at run-time.

An illustrative portion of the GENIE system is shown in the Appendix
25 D in the form of a Prolog source listing with comments. The following is further to the comments.

Process_sents with *get_inputsents*, *process_sects* and *outputresults* reads in an input stream, processes sections of the input stream according to parameter settings, and produces output according to the settings, respectively. Among
30 parameters supplied to *Process_sents* are the following: Mode (specifying the parsing

mode) and Protocol (html or plain). *Process_sents* is called by another predicate, after user-specified parameters have been processed.

The parsing modes are selected by GENIE so as to parse a sentence or phrase structure using a grammar that includes one or more patterns of semantic and syntactic categories that are well-formed. For example, for the phrase “bad inactivates jnk”, a legitimate pattern can be substance1 action substance2, wherein substance1 = protein bad, action = “inactivates” and substance2 = “jnk.” However, if parsing fails, various error recovery modes are utilized in order to achieve robustness. The error recovery techniques use methods such as segmenting the sentence, processing large chunks of the sentence, and processing local phrases. Each recovery technique is likely to increase sensitivity but decrease specificity and precision. Sensitivity is the performance measure equal to the true positive rate of the natural language processing, *i.e.*, the ratio of information extracted by the natural language processing system that should have been extracted. Specificity is the performance measure equal to the true negative information rate of the system, *i.e.*, the ratio of information not extracted by the NLP system that should not have been extracted. Precision is the reliability of the system, *i.e.*, the ratio of information extracted correctly compared to all the information that was extracted. In processing a report, the most specific mode is attempted first, and successive less specific modes are used only if needed.

In accordance with the preferred embodiments of the present invention, the parser of Figure 2 includes five parsing modes, Modes 1 through 5, for parsing sentences or phrases. Nominally, the parser is configured to first select Mode 1. If Mode 1 is not possible, the program continues with Mode 2 and so forth until parsing is complete. With Mode 1, the initial segment is the entire sentence and all words in the segment must be defined. This mode requires a well-formed pattern for the complete segment.

Mode 2 requires that the sentence or phrase be segmented at certain types of words or phrases, *e.g.*, “ is attributable to.” Here, an attempt is made to recognize each segment independently, *i.e.*, a first segment ending with the word “is” and a second segment beginning with the word after “to.” The segmenting process is

repeated until an analysis of each segment is obtained or until segmenting is no longer possible.

Mode 3 requires a well-formed pattern for the "largest" prefix of the segment, *i.e.*, usually at the beginning of the segment. This occurs when a sentence
5 contains a pattern at the end which is not in the grammar but a beginning portion that is included. For example, in "bad inactivates jnk at this time", the beginning of the sentence "bad inactivates jnk" will be parsed and the remainder will be skipped.

Mode 4 requires that undefined words be skipped and an analysis be attempted in accordance with Mode 1. Mode 4 is useful where there are
10 typographical errors and unknown words. For example, in the phrase "abc bad inactivates jnk", the word *abc* is unknown to the system and will be ignored but the remainder of the phrase will be parsed.

Mode 5 first requires that the first word or phrase in the segment associated with an action be found. Next, an attempt is made to recognize the phrase
15 starting with the leftmost recognizable argument. For example, in "during bad inactivates jnk on the fifth day," the phrase "bad inactivates jnk" will be parsed and the remaining words will not be. If no analysis is found, recognition is retried at the next possible argument to the right. This process continues until an analysis is found.

Process_sects with *get_section* and *parse_sentences* gets each section
20 and generates intermediate output for the sentences in each section.

Write produces the output as a list consisting of relations and interactions

Setargs sets arguments or parameter values based on user input or by default.

25 The structured output generated by the GENIE program uses a frame-based representation. Each frame specifies the informational type, the value, and arguments or modifier slots which are also frames. Consider the text data input "bad inactivates the phosphorylation of jnk." A corresponding output, as shown below, is a frame denoting an action, which has the value *inactivate*; in addition, there are two
30 arguments. The first argument is a protein *bad* and the second argument is an action with the value *phosphorylate*, which has two arguments. The first argument is *x*

signifying that the agent has not been specified; the second argument is a protein with the value jnk. The second argument is the target:

[action,inactive,[protein,bad],[action,phosphorylate,x,[protein,jnk

In summary, a computer system has been disclosed that generates
5 structured information concerning protein and gene interactions and relationships.

5.2. USE OF BLAST FOR FINDING GENE AND PROTEIN NAMES IN JOURNAL ARTICLES

In a specific embodiment of the invention, an exhaustive list of gene
and protein names, extracted from GeneBank, is translated into a different alphabet
10 system by substituting each character in the name with a predetermined unique
nucleotide combination. The encoded names are then imported into the BLAST
database using the FASTA format. The scientific journals are translated, using the
same nucleotide combinations, into a continuous string of nucleotides. A query is then
used to match the translated journals against the nucleotide representation of gene and
15 protein names in the BLAST database. Significant alignments associated with gene
and protein names are listed in the BLAST output file, which is subsequently
processed using Perl-scripts. The final result consists of the original journal article
with XML tags surrounding the gene and protein names.

To adapt the problem to BLAST's statistical foundation, different
20 measures were undertaken to limit the output to the most relevant gene and protein
names. In addition, in order to fine-tune the matching process, different BLAST
parameters were adjusted, such as the *word size* (which sets the size of the high
scoring words, thus influencing the sensitivity of finding HSPs) and *mismatch penalty*
(exact vs approximate matching).

25 In a specific embodiment of the invention, gene and protein names are
extracted from GeneBank's gene symbol index file. The following is an excerpt of the
file after discarding entries that are either composed of only numbers or of less than
two alphabetic letters:

gfap gamma
30 hox a10

hox a1
 wac 3'-end
 pit-1/ghf-1 variant
 [...]

5 This list of gene and protein names is translated into a different
 alphabet system by substituting each character in the name with a predetermined
 unique nucleotide combination. The conversion chart is listed in Appendix E. The
 encoded names are then imported into the BLAST database using the FASTA format.
 For example, the first entry in the list above is "gfap gamma." After translation using
 10 the conversion chart, the same name appears as follows:

AGCAACTAAACACCCATCCAAGCAAACACACACACAAAC

Thus, the complete FASTA entry looks like this:

>gi|1 species,gp,gfap gamma

AAGCAACTAAACACCCATCCAAGCAAACACACACACAAAC

15 In FASTA, the definition line (marked with '>') contains information
 about the database entry. This line can contain any kind of information. The
 information important for this particular example is the third entry in the definition
 line, 'gp', that specifies that the name can represent a gene *or* a protein. If the name is
 unambiguous, then the definition line states that the name is only associated with a
 20 gene ('g') or protein ('p'). The fourth entry in the definition line is the name of the
 protein or gene, "gfap gamma" in this case.

The second line in the FASTA format normally contains the actual
 sequence of the protein/gene. In the example presented, the second line contains the
 translated protein or gene name.

25 All gene and protein names are translated into the nucleotide
 representation and converted into the FASTA format. Then, the database containing
 these FASTA entries are specially compiled for use in BLAST queries using a
 program that is included in the BLAST package called "formatdb".

30 Thus, the scientific journals are translated, using the same nucleotide
 combinations, into a continuous string of nucleotides. For example, the sentence "In

the absence of costimulation, T cells activated through their antigen ..." is translated into

"AAGTACAGATCCACGGAAGGAACGATCCAAACAAAGACGCAACGACAG
AAATAACGATCCACATAACTATCCAAATACATACGCACGGAAGTACACAC
5 GTAATTAAACACGGAAGTACATACAGATCCATCCACGGATCCAAATAACG
AATTAATTACGCATCCAAACAAATACGGAAGTACTCAAACACGGAACGAA
CCATCCACGGAAGGACCTACATACGTAAGCAAGGATCCACGGAAGGAAC
GAAGTACCTATCCAAACACAGACGGAAGTAAGCAACGACAGATCC "

A query is then used to match the translated journals against the
10 nucleotide representation of gene and protein names in the BLAST database. The
query is executed using the blastall program that is included in the BLAST package.
The query line looks like:

```
blastall -p blastn -d FASTA.dat -i query.txt
```

The flag 'p' denotes the sub-program (blastn is a sub-program of
15 blastall that performs nucleotide matches), 'd' denotes the file that contains the
FASTA entries and 'i' denotes the translated query text.

Significant alignments associated with gene and protein names are
listed in the BLAST output file. This is an excerpt from a BLAST output file:

```
gi|63624 species,gp,ner
20 Length = 12
Score = 24.4 bits (12), Expect = 3e-05
Identities = 12/12 (100%)
Strand = Plus / Plus
Query: 729 acagaacgacct 740
25 Sbjct: 1 acagaacgacct 12
```

The first line denotes the database entry. The second line denotes the
database sequence length, followed by the alignment score and the E-value. The next
line indicates paired matches, mismatches and gapped alignment (the latter two are
not shown in this example). The lines 'Query' and 'Sbjct' show the actual alignment
30 between the query and database sequence. This output file is subsequently processed

using a Perl-script (see Appendix F). The script shown in Appendix G scans the output file, which is sometimes several megabytes long, for any segments that start at position 1 of the database sequence (thus disregarding any segments that are only part of the sequence). In addition, the script allows for 10% mismatches between the
 5 aligned sequences for long sequences (as shown in the script of Appendix E), or 0% mismatches for short sequences. After scanning the output file, an intermediary file that lists the candidate sequences is created:

```

      tran|365|381|gp|18493
      tran|1|17|gp|18493
10     peci|549|565|gp|58106
      il-2|621|637|gp|82396
      il-2|325|341|gp|82396
      gati|193|209|gp|92088
      prod|641|657|gp|52292
15     rap1|105|121|gp|49898
      spec|545|561|gp|33183
      crip|385|401|gp|118905
      crip|21|37|gp|118905
      as|161|177|gp|133961
20     her|65|77|gp|88411
  
```

The intermediary file lists the name of the sequence, followed by the starting and end point in the query sequence (corresponds to where the two sequences matched), the semantic class of the name (protein, gene or protein/gene). The last number is not considered.

25 The intermediary file is then scanned by another Perl program (Appendix G). This program compares the starting end points with the actual text, making sure that the matched name is an 'autonomous' entity in the query text. For example, while "per" in " per gene" should be recognized as a gene name, "per" in "personal" should not be recognized as a gene name. The program recognizes other
 30 characters than the space character delimiting an 'autonomous' gene or protein name.

In addition, the script looks for plurals of words. For example, "interleukins" should be recognized as a protein name, although only the singular form, "interleukin", is in the database.

The final result consists of the original journal article with XML tags surrounding the gene and protein names. This is done using the same script as in Appendix G:

blocked <phr sem="gp">T cell antigen receptor</phr> (TCR)- and
<phr sem="gp">CD28</phr>-mediated <phr sem="gp">IL-2</phr> gene
transcription. Therefore, <phr sem="gp">Rap1</phr> functions as a negative
regulator of...

To adapt the problem to BLAST's statistical foundation, different measures were undertaken to limit the output to the most relevant gene and protein names.

BLAST is sensitive to the search space the program works in. Thus,
given a long query sequence and a large sequence database, matches have a lower
statistical significance because the chances are higher that the matches could have
occurred by chance alone. In addition, matches with few letters have a lower statistical
significance than matches with many letters. In order to find all true matches with any
significance level, some measures were undertaken to address this problem. For
example, (i) the query sequence was divided into 10 equal length parts, *i.e.*, the
journal article was divided into 10 parts and 10 different queries are run on each part
separately; (ii) the sequence database (with the gene and protein names) is separated
into 5 databases, each containing protein/gene names of different length; (iii) gene
and protein names with less than 3 letters in the database were 'expanded', *i.e.*, spaces
were added at the beginning and the end of the name. Doing so, the statistical
significance of a match containing a short name was higher. A space does not only
include an empty character. For example, a gene name "k4" could occur in a journal
article as "kinin 4 (k4)". It was therefore important to define several characters as
substitutes for a space character. The alphabet in Appendix E defines the nucleotide
combination ATCC as such a substitute.

Working with nucleotides implies that errors involving reading frames must be addressed. For example, working with a code of four letters, the nucleotide combination ATCTGTCACG could mean ATCT/GTCA or TCTG/TCAC or CTGT/CACG . Since the text is translated into a nucleotide combination, only one of these possibilities is correct. But BLAST can not distinguish between these solutions,
5 *i.e.*, BLAST would potentially match a database sequence to a wrong reading frame in the query sequence, producing many nonsense results that could compromise the significance of true results.

The solution to this problem is a comma-free code. A comma free code
10 knows only one correct reading frame. BLAST therefore does not produce any nonsense results. A comma-free code consists of only one permutation of a nucleotide combination. For example, given the nucleotide combination ATCC and its permutations CATC, CCAT and TCCA, only ONE of these permutations would be included in a comma-free code. The code in Appendix E does represent a comma free
15 code. Comma-free codes were discussed in the early days of DNA research (Crick et al., Proc. Natl. Acad. Sci. 43:416-421).

In order to fine-tune the matching process, different BLAST parameters must be adjusted, for example: *word size* (which sets the size of the high scoring words, thus influencing the sensitivity of finding HSPs); *mismatch penalty*
20 (exact vs approximate matching); *numbers of alignments to show* (true matches of low significance can sometimes be at the very end of the BLAST output, therefore many alignments have to be shown); and *expectation value* (which sets the significance value for matches in the output file).

5.3. GENERATION OF SPECIALIZED DATABASES

25 In accordance with the present invention, specialized databases may be developed that contain information derived from unpublished data, publications such as research articles, theses, posters, abstracts, etc. and/or databases concerning interactions among genes and proteins, their domain/motif structure, and their biological functions.

For example, but not by way of limitation, a specialized database may be prepared as follows. Protein and gene sequences may be provided, for example, by the Java program PsiRetrieve which allows for quick retrieval of protein or nucleotide sequences from binary BLAST databases by sequence accession number, keyword or groups of keywords, or species name. In addition, using the program PsiRetriever, sequences encoding the proteins of interest may be retrieved from the non-redundant (NCBI) database of protein sequences and stored as a FASTA file. The FASTA file is then converted into a binary blast database using the program FORMATDB from the BLAST suit of programs.

Known motifs/domains for proteins may also be collected using the flat file versions of major protein databases, such as SwissProt (<http://expasy.hcage.ch/sprot>) and the non-redundant database of NCBI (<http://www3.ncbi.nlm.nih.gov>). The databases can be downloaded and searched for the keywords "motif" and "domain" in the feature tables of proteins. In addition, existing databases of motifs and domains, such as BLOCKS (<http://dupsas.Weizmann.ac.il/bcd/bcdparent//databanksblocks/hfml>) and pfam(<http://www.sanger.ac.uk//software/pfam>; <http://pfm.wustl.edu>), can be downloaded (Henikoff et al., 1991, NAR 19:6565-6572). Still further, it is understood that any publically available database containing gene/protein sequences may be utilized to generate the specialized databases for use in the practice of the present invention.

Homologous sequences may be aligned using, for example, the CLUSTALW program (Higgins, et al. 1996 Methods in Enzymology 266: 383-402). A protein's sequence corresponding to each domain/motif can be identified, saved and used for building a Hidden Markov Model (HMM) of the domain/motif using a HMMER and HMMER2 packages (see, Durbin, R. et al. 1998 in Biological Sequence Analysis: Probablistic Models of Proteins and Nucleic Acids). HMMER and HMMER2 packages are useful for (i) building HMMs from sets of aligned protein or nucleotide sequences, and (ii) comparing the HMMs with sequence databases aimed at identifying significant similarities of HMMs with database sequences. Both nucleotide and protein databases can be used for this purpose. Alternatives to the

Hidden Markov Model method for building domain/motif models include neural network motif analysis (Wu, C.H. et al., 1996, Comput Appl Biosci 12, 109-18; Hirst, J.D., 1991, Protein Eng 4:615-23) and positional weight matrix analysis (Claverie, J.M., 1994, Comput Chem 18:287-94; Venezia, D., 1993, Comput Appl Biosci 9:65-9; Bucher, P. 1996, Comput Chem, 20:3-23; Tatusov, R.L., 1994, Proc Natl Acad Sci USA 91:12091-5).

Once a comprehensive collection of motifs/domains is created, each particular protein may be compared against a complete database of HMMs to identify known motifs and domains.

10 The Hidden Markov Model (HMM) is built using the following steps:

- A1. Start with a motif/domain name and a single amino acid sequence representing a domain or motif.
- A2. Do PSI-BLAST (BLASTPGP) search with the motif/domain sequence against a protein non-redundant database.
- 15 A3. Retrieve the sequences identified in the database search from the protein sequence database. Exclude low-complexity sequences, short or incomplete sequences and sequences with similarity score above a selected threshold of PPD value <0.001
- A4. Align the set of sequences with CLUSTALW (or other multiple sequence alignment program).
- 20 A5. Use the set of aligned sequences for building HMM with the programs provided with HMMER and HMMER2 packages (see Hughey and Krogh 1996, J. Mol. Biol. 235:1501-1531).
- A6. Do a new database search comparing new HMM with the non-redundant protein database.
- 25 A7. Continue steps A3-A6 until the convergence of the Markov model *i.e.*, until no new sequences are identified, or the maximum allowed number of iterations as defined by the user is reached. (Hugh R. and Krogh A., 1996, Comput. Appl. Biosci. 12: 95-107).

30 In addition, in yet another embodiment of the invention, a specialized database may be designed to contain a semantic model of proteins and of the possible

interactions between them. Such databases are particularly useful for computation and analysis of regulatory networks between proteins. The semantic model is designed for representing substances, such as proteins and actions between them, and is based on widely accepted principles of object-oriented programming languages such as Java.

5 Figure 3 is a diagram illustrating the object representation of molecules and relations between them. As indicated in Figure 3 there are six major classes, corresponding to the top-level classification of objects and actions: (i) a substance; (ii) a state of a substance; (iii) a similarity between substances; (iv) an action between substances; (v) a result of the action; and (vi) a mechanism that enables an action.

10 Figure 3 presents the class design graphically, listing the variables that represent the properties of each class or class object in the implementation. Classes can be made nested via the mechanism of "inheritance", *i.e.*, classes are defined starting with the most general ones and moving towards more specific classes. Definition of more specific classes is simplified because the properties of the general
15 classes are "inherited" by the specific classes and need not be redefined each time (see, Flanagan 1997, Java in a Nutshell, Second Edition. O'Reilley & Associates, Inc. Sebastopol, CA).

As shown in Figure 3, the two key object types in this scheme are substances (nodes of the graph representing regulatory networks) and actions
20 (oriented edges connecting pairs of nodes), while result and mechanism objects are auxiliary to object action. Each substance object is characterized with a state. In this scheme, action is the most complicated object; each action object is characterized by a specific pair of substances participating in the action, one of which can be active and is referred to as Subject Substance and the second of which can serve as a substrate for
25 the former and is referred to as Object Substance. Furthermore, for each action the initial and final states corresponding to interacting substances are defined. The property Time Required of each Action Object allows the setting of different durations for different actions (time is measured in relative units; see René Thomas and Richard D'Ari, 1990, "Biological Feedback," CRC Press Boca Raton, Ann Arbor,
30 Boston).

Once developed, the specialized databases can be used to identify novel genes based on computation and analysis of phylogenetic trees for multigene families and analysis of homologous regulatory networks.

In a specific embodiment of the invention, a specialized database was generated using a set of keywords defining proteins involved in apoptosis (see, Figure 4). The specialized sequence database was referred to as Apoptosis 3. As a first step in generating the specialized database, a comprehensive set of articles describing the system of apoptosis or programmed cell death was compiled. The articles were analyzed and information on regulatory pathways characterizing apoptosis from a variety of different organisms was extracted. Such pathways included those involved in MHC-T cell receptor interactions, inflammatory cytokine signal transduction, induction by light, γ -radiation, hyperosmolarity or heat shock, pathways involving immunoregulatory receptors or receptors having cytoplasmic domains, integrin-related pathways and perforin/granzyme β related pathways. The collected information was stored using Powerpoint (Microsoft) as a collection of graph/plots depicting the regulatory pathway. In addition, a list of proteins relevant to regulation of apoptosis was compiled.

Using the program Psi Retriever, sequences encoding the proteins relevant to regulation of apoptosis were retrieved from the non-redundant (NCBI) database of protein sequences and stored as a FASTA file. The FASTA file was then converted to a binary blast database using the program FORMATDB from the BLAST suit of programs. The BLAST suit of programs provides a set of programs for very fast comparisons of a single sequence to a large database. Both the database and the search or query sequence can be any combination of nucleotide and/or amino acid sequences.

In a working example described herein, the Apoptosis 3 database was used to compare genomic and cDNA sequences derived from the 13q region of human chromosome 13. This region of the chromosome is associated with Chronic Lymphocytic Leukemia (CLL). Using this method of analysis a human gene with significant homology to the mouse Rpt1 gene was identified. When the activity of Rpt1 is knocked out in mice, the regulatory effect is manifested as a block in T-

lymphocyte apoptosis. This result indicates that the identified human Rpt1 homology may represent the gene in which genetic defects lead to CLL.

The amino acid sequence of the human Rpt1 gene is presented in Figure 15. The present invention relates to nucleic acid molecules encoding the human Rpt1 protein shown in Figure 15. The invention also relates to nucleic acid molecules capable of hybridizing to a nucleic acid molecule encoding the human Rpt1 protein presented in Figure 15 under conditions of high stringency. By way of example and not limitation, procedures using such conditions of high stringency are as follows: Prehybridization of filters containing DNA is carried out for 8 hours to overnight at 65°C in buffer composed of 6x SSC, 50 mM Tris-HCl (pH7.5), 1mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA and 500 mg/ml denatured salmon sperm DNA. Filters are hybridized for 48 h at 65°C in prehybridization mixture containing 100mg/ml denatured salmon sperm DNA and 5-20 x 10⁶ CpM of ³²P-labeled probe. Washing of filters is done at 37°C for 1 h in a solution containing 2x SSC, 0.01% PVP, 0.01% Ficoll and 0.01% BSA. This is followed by a wash in 0.1 x SSC at 50°C for 45 minutes before autoradiography. Other conditions of high stringency which may be used are well known in the art.

5.4. GENE DISCOVERY THROUGH PHYLOGENETIC ANALYSIS OF GENE FAMILIES

The present invention provides a method for identifying novel genes comprising the following steps: (i) comparing a single sequence with a database; (ii) processing the output into a sequence alignment; (iii) computing gene trees; and (iv) analyzing the trees to predict the existence of undiscovered genes.

Figure 5 shows a "species tree," a "gene tree" and a "reconciled tree". A "species tree", as defined herein, is a graph depicting the correct order of speciation events leading to a set of present day species as defined by taxonomy. A "gene tree" is a graphical representation of the evolution of a gene from a single ancestral sequence in a common progenitor to a set of present-day sequences in different species. Where gene duplication has occurred, a branch is bifurcated. The branch lengths of a gene tree are most frequently measured either in terms of the number of

amino acid or nucleotide replacements per site or in terms of millions of years (absolute geological time). In the former case, the average replacement rate in the majority of the published trees varies among tree branches, and the root-to-tip distances are different for different present day sequences. In the latter case, all root-to-tip distances are equal and the height of each interior node of the tree corresponds to the absolute geological time passed since the gene duplication corresponding to the interior node took place.

If a gene is unique, *i.e.*, represented with a single copy per genome rather than being a member of a family of similar genes, the correct gene tree depicting the origin of this gene in a few different species is identical to the species tree. In many instances, a single ancestral gene has been duplicated repeatedly during evolution to form a multigene family. A gene tree is constructed from a gene as it occurs in several species and reflects both speciation events and gene duplications within the same genome. Two homologous genes taken from different species that originated from the nearest common ancestor by speciation are referred to as orthologs, while any two genes that originated from the common ancestor via a series of events involving intragenomic duplications, or conversions, are called paralogs. The terms "ortholog" and "paralog" are applied to both nucleic acid and proteins herein.

If gene deletions are forbidden and all genes for all species represented in the tree are known, the gene tree can be reconfigured to recapitulate the species tree, such that each subtree contains only orthologous genes. This tree is referred to as a reconciled tree and is shown in Figure 5. Imperfect gene trees which contain incorrect or partial species subtrees can be used to build reconciled trees that indicate events of speciation, gene loss, and gene duplication.

Orthologs from different species in gene trees are usually clustered together, so that if all the existing homologous genes from different species were known, the same relationship of species would be recapitulated in each cluster of orthologous genes. Since in reality a considerable number of genes are not yet identified, the real gene trees contain incomplete clusters of orthologs that can be used for identification of the missing genes.

By applying phylogenetic analysis, *i.e.*, reconstruction of gene trees of gene/protein sequences, one can predict the existence of undiscovered genes in humans and other species in addition to identifying the function of a gene. Such a technique is a significantly more powerful tool for identification of new genes than
5 mere sequence comparisons.

Methods of computing gene trees from a set of aligned sequences include the : (i) heuristic method based on an optimization principle which is not directly motivated by a probability model (Fitch, 1974 J. Mol. Evol. 3:263-268)), (ii) the maximum likelihood method (Goldman, 1990, Syst. Zool. 30:345-361; Yang et
10 al., 1995, Syst. Biol. 44:384-399; Felsenstein, J., 1996, Methods Enzymol. 266-418-427); and (iii) the distance matrix tree making method (Saito, N. and Nei, M., 1987, Mol. Biol. Evol. 4:406-425). Since the data analyses of orthologs and paralogs often involve very distantly related sequences, the maximum likelihood method is preferably used for small data sets and the distance-matrix method in other instances.

15 To construct a reconciled tree according to the invention, the first step comprises a search for homologs in a publicly or privately available database such as, for example, GenBank, Incyte, binary BLAST databases, Swiss Prot and NCBI databases. Following the identification of homologous sequences a global alignment is performed using, for example, the CLUSTALW program. From the sequence
20 alignment a gene tree is constructed using, for example, the computer program CLUSTLAW which utilizes the neighbor-joining method of Saito and Nei (1997, Mol. Biol. Evol. 4:406-425). Construction of a species tree is then retrieved from, for example, the following web site:

<http://www3.NCBI.NLM.NIH.GOV//taxonomy.tax.html>.

25 The species tree and gene tree are given as input into the algorithm described below, which integrates both trees into a reconciled tree. Agreement between the gene tree and the corresponding species tree for any given set of sequences indicates the identification of orthologs. In contrast, disagreement between the species and gene tree suggest a gene duplication that resulted in the formation of a
30 paralog. Thus, through generation of a reconciled tree one can identify orthologs present in one species but missing in another. These can be deduced by forming

subtrees of orthologs in a gene tree, and then comparing the subtree in the gene tree with a species tree. A missing gene appears as a branch present in the species tree but absent in the gene tree. The algorithm for defining an orthologous gene subtree and predicting the undiscovered, or lost in evolution, genes is as follows:

- 5 Let T_g be the most likely gene tree identified with one of consistent tree-making methods from a set of properly aligned homologous genes $\{1, 2, \dots, s\}$, such that one or more homologous genes from every species corresponds to pending vertices of T_g . Each gene is labeled with the species it comes from $(1, \dots, s)$ adding subscripts to distinguish homologous genes from the same species whenever it is necessary. Let T_s be the true species tree (tree correctly reflecting speciation events which we assume to be known) for species $\{1, 2, \dots, s\}$. Due to the biological meaning of T_s each species in this tree is represented only once. It is assumed that both T_s and T_g are binary, although it is straightforward to extend the algorithm described here to the case of multifurcated trees.

15 Algorithm

- A1. For each pair of interior nodes from trees T_g and T_s , compute similarity $\sigma(S_{gi}, S_{sj})$.
- A2. Find the maximum $\sigma(S_{gi}, S_{sj})$.
- A3. Save S_{gi} as a new subtree of orthologs, save $\{S_{gi}\} - \{S_{sj}\}$ as a set of species that are likely to have gene of this kind (or lost it in evolution).
- 20 A4. Eliminate S_{gi} from T_g ; $T_g := T_g \setminus S_{gi}$.
- A5. Continue A2 - A4 until T_g is non-empty.

The following definitions apply:

- Let S_{gi} be an i th subtree of T_g (corresponding to the i th interior node),
 25 correspondingly, let S_{sj} be j th subtree of tree T_s .
- Let $\{S_{gi}\}$ stand for an unordered set of species represented in S_{gi} such that each species is represented exactly once, and let $|\{S_{gi}\}|$ and $\{|S_{gi}|\}$ be the number of entries in $\{S_{gi}\}$ and the number of pending vertices in S_{gi} , respectively. Define by $S_{sj}(S_{gi})$ the unique subtree of S_{sj} that has leaves labeled exclusively with species from
 30 $|\{S_{gi}\}|$, so that each element of $|\{S_{gi}\}|$ is used i.e., that is, the unique subtree obtained by eliminating from S_{sj} all species that are not present in $|\{S_{gi}\}|$.

Then define similarity measure, σ , between S_{gi} and S_{sj} in the following way:

$\sigma(S_{gi}, S_{sj}) = 0$ if $|S_{gi}| \neq |\{S_{gi}\}|$, or $S_{sj}(S_{gi}) \neq S_{gi}$, and

$$\sigma(S_{gi}, S_{gi}) = |S_{gi}|$$

The support of tree clusters by data can be measured using the bootstrap technique
5 described in Felsenstein (1985, Evolution 39:783-791).

In an embodiment of the invention, the human antiquitin gene was identified using phylogenetic analysis. The aldehyde dehydrogenase gene family in humans can be subdivided into at least ten ancient subtrees characterized by different functions of corresponding proteins. These genes probably arose from a series of gene
10 duplications of an ancestral gene which took place before the divergence of a common ancestor of Eukaryotes and Eubacteria.

The aldehyde dehydrogenase gene cluster is highlighted in Figure 6 which shows the original tree of ALDH sequences, the circled area indicating a sequence cluster where bacterial (*Bacillus subtilis*), plant (*Brassica napus*), and
15 nematode (*Caenorhabditis elegans*) ortholog is present, but a human ortholog is not known. A random screening of cDNA libraries showed that a human ortholog, referred to as antiquitin, does exist. Figure 7 shows the same gene tree as in Figure 6 with an additional human protein referred to as antiquitin present in the tree.

In yet another embodiment of the invention, a human ortholog of the
20 murine Max-interacting transcriptional repressor Mad3 was identified through phylogenetic analysis of a gene family. The gene tree was constructed as follows. The protein sequences of known members of the *Mad* gene family were extracted from GenBank database. The extracted sequences were aligned using multiple alignment program CLUSTALW running on Sun SPARC station. Redundant and
25 non-homologous sequences as well as distant homologs from *S. cerevisiae*, *C. elegans*, *D. melanogaster* etc. were removed from the alignment. The refined set of sequences were realigned with CLUSTALW and a gene tree as presented in Figure 18A was computed. To identify a human ortholog of the Mad3 protein, a human dbEST at NCBI was searched with program TBLASTN using mouse Mad3 protein
30 sequences as a query. Two highly homologous ESTs were identified and are presented in Figure 17A. To obtain a complete coding sequence a search was

conducted to obtain overlapping sequences in dbEST. The search for overlapping sequences was performed using the program Iterate with EST Zs77e55.rl (gb/AA278224) as the search query. The search identified a single overlapping sequence. The search for overlapping sequences was performed using program Iterate
5 with EST zs77e55.rl (gb/AA278224) serving as a query. The search returned a single overlapping sequence, namely HUMGS0012279 (dbj/C02407), thus showing that the two EST sequences found during the initial TBLASTIN search belong to the same gene. The complete sequence of the gene was assembled from the two ESTs using commercially available sequence assembly program SeqMan11 (DNASTAR Inc., WI).
10 The nucleotide sequence of the human Mad3 gene is presented in Figure 17B. The deduced amino acid sequence of which is presented in Figure 17C. The complete DNA sequence is also shown.

The present invention relates to nucleic acid molecules encoding the human Mad3 protein shown in Figure 17C. The invention also relates to nucleic acid
15 molecules that hybridize to the nucleic acid molecule of Figure 17B under conditions of high stringency and encode a Mad3 protein. By way of example and not limitation, procedures using such conditions of high stringency are as follows: Prehybridization of filters containing DNA is carried out for 8 hours to overnight at 65°C in buffer composed of 6x SSC, 50mM Tris-HCl (pH7.5), 1mM EDTA, 0.02% PVP, 0.02%
20 Ficoll, 0.02% BSA and 500 mg/ml denatured salmon sperm DNA. Filters are hybridized for 48 hours at 65°C in prehybridization mixture containing 100 mg/ml denatured salmon sperm DNA and 5-20 x 10⁶ CpM of ³²P-labeled probe. Washing of filters is done at 37°C for 1 hour in a solution containing 2x SSC, 0.01% PVP, 0.01% Ficoll and 0.01% BSA. This is followed by a wash in 0.1x SSC at 50°C for 45
25 minutes before autoradiography. Other conditions of high stringency which may be used are well known in the art.

5.5. SIMULATION AND HYPOTHESIS TESTING

The simulation and hypothesis testing methods of the invention, described in the subsections below, utilize specialized databases of gene/protein
30 structures and interactions for identifying potentially undiscovered members of

multigene families through comparisons of regulatory networks for different species, searching expressed sequence tag (EST) databases, and simulation of regulatory cascades.

5.5.1. GENE DISCOVERY THROUGH ANALYSIS OF REGULATORY NETWORKS

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The present invention provides a method for identifying undiscovered genes through comparisons of regulatory networks for different species where functionally similar regulatory systems are conserved. The amount of information available concerning regulatory genes and/or proteins in different organisms and their functional relationships allows one to reconstruct and compare regulatory networks. Since in most cases, the knowledge of all genes involved in almost any particular regulatory system is incomplete, a comparison of homologous networks within the same organism and between different species permits the identification of genes absent in a system under comparison.

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The identified genes, being part of a regulatory network, are implicated as potentially contributing to a phenotype of a disease associated with the system under analysis. Using the methods of the present invention these putative disease genes can be cloned, mapped and analyzed for mutations directly, thereby omitting the expensive and time-consuming steps of positional cloning and sequencing of genomic regions. Gene discovery by analysis of regulatory networks is outlined in Figure 8. The analysis is initiated starting with a biological system (*e.g.*, signaling pathway of genes involved in Bcl-2-regulated apoptosis in lymphocytes), a single gene (*e.g.*, Bcl-2) or a gene family (*e.g.*, caspases).

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Initially, a specialized database is generated for comparison of regulatory networks between different species. For example, starting with a single candidate gene in a single species, a typical iteration in this process begins with identification of all known proteins and genes that are upstream and downstream with respect to it in regulatory hierarchies and the reconstruction of a network of interacting genes and proteins. Next, for each protein, a set of key domains and motifs is identified and this information is used to search for related proteins in humans and

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other species. The identified sequences are compared and for each pair of sequences showing similarity above a certain threshold, a similarity object is generated. A similarity object is generated if two sequences, nucleotide or amino acid, show significant similarity in database searches (p value < 0.001). The object retains the following information: (i) reference to similar substances *i.e.*, genes or proteins; (ii) significance of the similarity, similarity score and percent of identity; and (iii) coordinates of the similarity region within two compared sequences.

"Orthology objects" constitute a subset of "similarity objects" which satisfies one additional requirement, *i.e.*, that two similar sequences should be identified as orthologs by the tree-based algorithm described above. In identifying orthologs, if gene A is orthologous to gene B, and gene B is orthologous to gene C, gene A is necessarily orthologous to gene C.

In a specific embodiment of the invention, for each species under analysis, orthologous proteins or genes are identified. In a further embodiment of the invention, small orthologous molecules participating in a regulatory network for two or more species may also be identified. Where proteins, genes, or molecules are orthologs, the action of the protein, gene or molecule between species may be interchangeable. If more than two species are involved in the analysis, subtrees of orthologous substances and subtrees of orthologous actions are identified.

Once orthologous genes, proteins or molecules are identified in two or more species, by forming a reconciled tree, for example, a set of orthologous or paralogous regulatory networks can be analyzed and visualized using graph theory where arcs represent actions and vertices represent substances. Thus, the method of the invention may further comprise the following steps: (i) superimposing the orthologous regulatory networks from two or more species and searching for the actions (arcs) and substances (vertices) in the homologous networks that are represented in some taxa but absent in others; (ii) superimposing paralogous regulatory networks from the same taxa and searching for paralogous genes that are missing in some taxa; and (iii) computing a general regulatory network that summarizes common regulatory sequence relationships known for more than one species.

In a specific embodiment of the invention a set of regulatory networks from different species, relating to the same biological system, apoptosis, for example, can be analyzed and visualized utilizing the following methods: (i) for each species functional information is collected relating to apoptosis; (ii) using the functional information, regulatory networks for each species comprised of interacting proteins and/or the genes involved in apoptosis are generated; (iii) the sequences of the interacting proteins and genes of each of the regulatory network are compared and for sequences showing similarity above a predetermined threshold range; and (iv) distinguishing between orthologs and paralogs using the methods set forth above.

An analysis similar to that performed using subtrees of sequences may be applied to classify protein functions as orthologous or paralogous actions. A "generalized" regulatory network maybe represented as a network wherein a substance as it occurs in a particular species is substituted with a cluster (i.e., subtree) of orthologous substances among species. In the final step of the analysis the clusters within each species are compared to one another, to identify missing genes.

Figure 11 depicts the regulatory relationships among hypothetical proteins (denoted with Arabic numerals) of hypothetical species A and B. As indicated in Figure 11A, an overlay of regulatory data for two species overlaps, but not completely. As indicated, protein 5 is known only for species B while protein 3 is known only for species A. The proteins in different species denoted with the same numeral are considered orthologous. As indicated, the regulatory relationships between a pair of proteins can be of three different kinds. Figure 9B, 9C, and 9D represent Boolean operations, OR, AND, and XOR, as arcs of the two regulatory relationships depicted in Figure 9A, the same operations being applicable to the set of vertices of the two regulatory relationships.

In some instances, orthologous networks in two distantly related taxa may have the same domains but arrangement of the domains between the related taxa may be different. In such a case, a one-to-one correspondence between orthologous proteins in closely related species has to be substituted with a one-to-many relationship among domains comprised within the proteins. For this purpose, a similarity object may be defined operating on pairs of motifs/domains in two proteins, and substitute pairs of

orthologous proteins with pairs of orthologous domains. After this correction, homologous networks are compared as described above.

Figure 10 is a diagram representing a hypothetical example of defining homologous protein networks in two different species using protein motifs, the diagram showing only two hypothetical proteins (lane 2) for species A and three hypothetical proteins (lanes 1, 3, and 4) for species B. Protein 1 in both species has motifs α and β , protein 2 has motifs δ , ϵ , and ζ , and proteins 3 and 4 have motifs δ and ζ , and ϵ , respectively. The motif analysis indicates that proteins 3 and 4 in species B may collectively perform the same function as protein 2 in species A.

10 5.5.2 GENE DISCOVERY BASED ON PROTEIN MOTIF/DOMAIN SEARCHES

The present invention provides yet another method for identifying genes that are homologous and perform the same or an analogous function in different species. The method of the invention comprises the following steps: (i) creating a database of sequences which comprise a motif or domain composition of a gene of interest using, for example, HMMER software; and (ii) searching additional databases for expressed sequence tags (ESTs) containing the domains and motifs characteristic for the gene of interest with HMMs of domains and motifs identified in step (i). In yet another embodiment of the invention, sequences may be searched which correspond to nucleotide sequences in an EST database or other cDNA databases using a program such as BLAST and retrieving the identified sequences. In an optional step, for each EST identified, sequence databases can be searched for overlapping sequences for the purpose of assembling longer overlapping stretches of DNA. Once identified, the ESTs can be used to isolate full length nucleotide sequences comprising the gene of interest using methods such as those described in Section 5.4, *infra*.

The general flowchart scheme for gene discovery analysis based on motif/domain search is shown in Figure 11. In a specific embodiment of the invention, the method referred to as the "phylogenetic reflection technique" comprises, first, defining the motif or domain composition of a gene of interest involved in a biological system of interest. Second, protein-coding genes from other species,

including for example yeast and/or nematode genes, that bear a significant similarity to the gene of interest or a specified domain of the corresponding protein are collected. Third, the identified genes are in turn subjected to a "domain analysis" to establish protein motifs which might suggest a function of these genes using, for
5 example, HMMER software. Fourth, the selected genes are in turn used for database searches in EST databases (dbEST) and/or a non-redundant (nr) database to identify unknown genes that are potentially orthologous to the selected yeast and nematode genes. Once identified ESTs having different tumor suppressor domains may be linked using multiple PCR primers. Using routine cloning techniques, well known to
10 those of skill in the art, a full length cDNA representing the gene of interest can be obtained.

Once new genes are identified by domain/motif analysis experimental searches may be carried out to isolate complete coding sequences and evaluate their tissue- and disease-specific expression patterns. In parallel their position with respect
15 to regulatory networks can be identified as described below.

In a specific embodiment of the invention, an apoptosis related human gene was identified using the method described above. As a first step *C. elegans* genes containing either POZ or Kelch domains were identified. A Hidden Markov Model was developed using POZ and Kelch sequences from the *Drosophila* Kelch
20 protein and any identified homologs. The resulting Hidden Marker Model was used to search through the collection of *C. elegans* protein sequences. One of the identified *C. elegans* genes contained a POZ domain, death domain, kinase domain and heat repeat. The presence of both a death domain and a kinase domain suggested that the protein functions as a regulatory protein.

25 A human EST database was searched using the protein sequence of the identified *C. elegans* gene and two sequences were identified (Figure 14A). A gene tree was computed to determine whether the identified human sequences were orthologs of the *C. elegans* gene. As depicted in Figure 14B, the human EST AA481214 appears to be a true ortholog of the *C. elegans* gene. Figure 14C presents
30 the nucleotide sequence of the identified death domain gene. Figure 14D presents the amino acid sequence of the death domain protein.

The present invention encompasses the nucleic acid molecule of Figure 14C, comprising the sequence of EST AA481214 and proteins encoded by said nucleic acid molecule. The invention also relates to nucleic acid molecules capable of hybridizing to such a nucleic acid molecule under conditions of high stringency. By way of example and not limitation, procedures using such conditions of high stringency are as follows: Prehybridization of filters containing DNA is carried out for 8 hours to overnight at 65°C in buffer composed of 6x SSC, 50mM Tris-HCl (pH7.5), 1mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA and 500 mg/ml denatured salmon sperm DNA. Filters are hybridized for 48 hours at 65°C in prehybridization mixture containing 100 mg/ml denatured salmon sperm DNA and 5-20 x 10⁶ CpM of ³²P-labeled probe. Washing of filters is done at 37°C for 1 hour in a solution containing 2x SSC, 0.01% PVP, 0.01% Ficoll and 0.01% BSA. This is followed by a wash in 0.1x SSC at 50°C for 45 minutes before autoradiography. Other conditions of high stringency which may be used are well known in the art.

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5.5.3. SIMULATION OF REGULATORY CASCADES

In an embodiment of the invention, an interactive graphical program is utilized for visualizing the scheme of regulatory relationships, "current" states of the substances, and active and inactive actions between pairs of substances. Such a program can be utilized for identification of genes which are associated with a specific disease. Currently, disease associated genes are discovered through positional cloning methods which combine methods of genetics and physical mapping with mutational analysis. The present invention provides a novel method for discovering disease associated genes. For simulating regulatory cascades, it is assumed that the time in a simulated regulatory system advances in discrete "quanta," or periods of time. The "state of substances" of the system for each discrete period of time is computed by: creating a set of substance objects, where a set of interactions between each created substance object is known, an initial state is specified. The time is initially set to zero. All defined actions are observed to confirm that the substances corresponding to the actions (i) exist, and (ii) are in the right initial states. Action is defined by a pair of substances that are in suitable states. The "subject" substance is in the inactive state,

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while the "object" substance can be in either active, or inactive, state depending on the action type. For example, the action "dephosphorylation" requires an active phosphatase ("subject" substance) and a phosphorylated substitute protein ("object" substance) in phosphorylated form. If both conditions are satisfied, the action is recorded as in progress. At termination, the substances must change their states as specified by the action. On each following "quantum" of time, the simulation proceeds in the same way while maintaining the "bookkeeping" of the remaining time for each action and the remaining lifespan of each substance. The simulation stops when there are no more active actions available. The program allows editing of the properties of the objects, changing the scale and focus of the visualized simulation, and experimenting with the systems output.

In a specific embodiment of the invention a "knock out" of a gene can be simulated to model the regulatory system that normally includes hypothetical gene A. One of the typical questions related to the gene knock out is how does the knock out affect a biological pathway of interest. A hypothetical example of evaluating the impact of a knock out of hypothetical gene A on the expression of a hypothetical gene B is shown in Figure 12. The answer to such a question could be "gene B will be inhibited" or "gene B will be induced" or "no effect".

In the practice of the present invention, a simple algorithm involving multiplication of gene interaction "signs" along the shortest pathway between the genes can be used to determine the outcome. The algorithm involves the following steps: (i) identification of the shortest non-oriented pathway connecting genes A and B involved in a pathway of interest; (ii) assigning sign "-" to gene A since it is knocked out and taking this sign as the initial sign value; (iii) moving along the shortest pathway between genes A and B, multiplying the current value of the sign with the sign of the next arc, where "-" stands for inhibition, "+" stands for induction or activation, and "0" stands for the lack of interaction between two proteins in the specified direction; (iv) determining if the final result of multiplication is "0", if so eliminating the zero arc and trying to find the shortest oriented bypass pathway between A and B in the remaining network; otherwise stop. The final value of the sign at the moment of arriving at vertex B would indicate the most likely effect of the

knock out of gene A which can be any one of the following: inhibition of gene B, induction/activation of gene B, or none. In addition to the "electronic knock out", an "electronic knock in" of a particular gene can be simulated. In such a computer simulation, the artificial addition of a gene and its effect on a regulatory system may
5 be analyzed.

5.6. IDENTIFICATION AND ISOLATION OF NOVEL GENES

The present invention relates to identification of novel genes, i.e., missing orthologs or paralogs, and the isolation of nucleic acid molecules encoding
10 novel genes. In a specific embodiment, a nucleic acid molecule encoding a missing ortholog or paralog can be isolated using procedures well known to those skilled in the art (See, for example, Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, 2d Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York Glover, D.M. (ed.), 1985, DNA Cloning: A Practical Approach MRL Press,
15 Ltd., Oxford, U.K. Vol. I, II.).

For example, genomic and/or cDNA libraries may be screened with labeled DNA fragments derived from a known ortholog or paralog from a specific species and hybridized to the genomic or cDNA libraries generated from a different species. For cross species hybridization, low stringency conditions are preferred. For
20 same species hybridization, moderately stringent conditions are preferred. Any eukaryotic cell potentially can serve as the nucleic acid source for the molecular cloning of the gene of interest. The DNA may be obtained by standard procedures known in the art from cloned DNA (e.g., a DNA "library"), by cDNA cloning, or by the cloning of genomic DNA, or fragments thereof, purified from the desired cell.

25 By way of example and not limitation, procedures using conditions of low stringency are as follows (see also Shilo and Weinberg, 1981, Proc. Natl. Acad. Sci. USA 78:6789-6792; and Sambrook et al. 1989, Molecular Cloning, A Laboratory Manual, 2d Ed., Cold Spring Harbor Laboratory Press, Cold Spring harbor, New York): Filters containing DNA are pretreated for 6 h at 40°C in a solution containing
30 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 mg/ml denatured salmon sperm DNA. Hybridizations are

carried out in the same solution with the following modifications: 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 mg/ml salmon sperm DNA, 10% (wt/vol) dextran sulfate, and 5-20 X 10⁶ cpm ³²P-labeled probe is used. Filters are incubated in hybridization mixture for 18-20 h at 40°C, and then washed for 1.5 h at 55°C in a solution
5 containing 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS. The wash solution is replaced with fresh solution and incubated an additional 1.5 h at 60°C. Filters are blotted dry and exposed for autoradiography. If necessary, filters are washed for a third time at 65-68°C and reexposed to film. Other conditions of low stringency which may be used are well known in the art (*e.g.*, as employed for
10 cross species hybridizations).

In another specific embodiment, a nucleic acid which is hybridizable to a nucleic acid under conditions of moderate stringency is provided. For example, but not by way of limitation, procedures using such conditions of moderate stringency are as follows: filters containing DNA are pretreated for 6 h at 55°C in a solution
15 containing 6X SSC, 5X Denhart's solution, 0.5% SDS and 100 mg/ml denatured salmon sperm DNA. Hybridizations are carried out in the same solution and 5-20 X 10⁶ CpM ³²P- labeled probe is used. Filters are incubated in the hybridization mixture for 18-20 h at 55°C, and then washed twice for 30 minutes at 60°C in a solution containing 1X SSC and 0.1% SDS. Filters are blotted dry and exposed for
20 autoradiography. Other conditions of moderate stringency which may be used are well-known in the art. Washing of filters is done at 37°C for 1 h in a solution containing 2X SSC, 0.1% SDS.

For expression cloning (a technique commonly used in the art), an expression library is constructed. For example, mRNA is isolated from the cell type
25 of interest, cDNA is made and ligated into an expression vector (*e.g.*, a bacteriophage derivative) such that it is capable of being expressed by a host cell (*e.g.*, a bacterium) into which it is then introduced. Various screening assays can then be used to select for the expressed gene product of interest based on the physical, chemical, or immunological properties of its expressed product. Such properties can be deduced
30 from the properties of the corresponding orthologs from other species.

In another embodiment, polymerase chain reaction (PCR) can be used to amplify the desired sequence from a genomic or cDNA library. To isolate orthologous or paralogous genes from other species, one synthesizes several different degenerate primers, for use in PCR reactions. In a preferred aspect, the
5 oligonucleotide primers represent at least part of the gene comprising known ortholog or paralog sequences of different species. It is also possible to vary the stringency of hybridization conditions used in priming the PCR reactions, to allow for greater or lesser degrees of nucleotide sequence similarity between the known nucleotide sequences and the nucleic acid homolog being isolated.

10 Synthetic oligonucleotides may be utilized as primers to amplify by PCR sequences from a source (RNA or DNA), preferably a cDNA library, of potential interest. PCR can be carried out, *e.g.*, by use of a Perkin-Elmer Cetus thermal cycler and a thermostable polymerase, *e.g.*, Amplitaq (Perkin-Elmer). The nucleic acids being amplified can include mRNA or cDNA or genomic DNA from any eukaryotic
15 species. After successful amplification of a segment of a the gene of interest, that segment may be molecularly cloned and sequenced, and utilized as a probe to isolate a complete cDNA or genomic clone.

Once identified and isolated the gene of interest can then be inserted into an appropriate cloning vector for amplification and/or expression in a host. A
20 large number of vector-host systems known in the art may be used. Possible vectors include, but are not limited to, plasmids and modified viruses, but the vector system must be compatible with the host cell used. Such vectors include, but are not limited to, bacteriophages such as lambda derivatives, or plasmids such as pBR322 or pUC plasmid derivatives or the Bluescript vector (Stratagene). The insertion into a cloning
25 vector can, for example, be accomplished by ligating the DNA fragment into a cloning vector which has complementary cohesive termini.

6. EXAMPLE: USE OF SPECIALIZED DATABASES FOR IDENTIFICATION OF NOVEL GENES

To test the method of using databases for gene discovery, protein
30 sequence and domain/motif databases specific to two overlapping functional

groupings of proteins: (i) proteins known to be tumor suppressors, and (ii) proteins implicated in apoptosis in animals were developed.

6.1 APOPTOSIS GENE DISCOVERY METHOD

5 Identification of a putative apoptosis-related human gene began with an identification of all genes in *C. elegans* that contained either a POZ or kelch domain. A subset of these genes is shown in Figure 13. Hidden Markov Models (HMM) for the POZ and Kelch domains were built as follows. Starting with POZ and kelch sequences from the *Drosophila* kelch protein (gi|577275) homologs were
10 identified in other protein sequences using the BLASTP program. The resulting sequences showing significant similarity (e-value less than 0.001) were aligned using CLUSTALW program and the alignments were used to build Hidden Markov Models with HMMER-2 package (Krogh et al., 1995, :<http://hmmer.wustl.edu/>). A computer printout listing of HMM models of tumor suppressors appears as a Microfiche H to
15 the present specification. (See, <http://hmmer.wustl.edu/>; Chapter 2, which is incorporated by reference herein in its entirety, for a detailed description of HMM models)

The resulting models were used to search through a database collection of *C.elegans* protein sequences. The domain structures of proteins having either a
20 POZ or kelch domain were identified using existing collections of protein domains (e.g., see [http://blocks.fhcrc.org/blocks/blocks release.html](http://blocks.fhcrc.org/blocks/blocks%20release.html), <http://coot.embl-heidelberg.de/SMART/>, <http://www.motif.genome.ad.jp/>). One of the unannotated protein-coding genes of *C. elegans* (corresponding protein accession number gi|1132541, see Figure 11) appeared to include a POZ domain, death domain, kinase
25 domain, and heat repeat. A death domain is characteristic for the apoptosis system and a kinase domain indicates that the protein is likely to participate in phosphorylation of other proteins. The presence of these particular domains suggests that this protein is serving as a regulatory protein.

Using the protein sequence of gi|1132541, the database of human EST
30 sequences was searched and a number of partial human cDNA sequences representing potential human orthologs or paralogs of the *C.elegans* gi|1132541 were identified.

The two closest human sequences, AA481214 and W51957, are depicted in Figure 14A. To determine whether the identified human sequences were orthologs or paralogs to the gi|1132541 gene of *C. elegans*, a gene tree (Saito and Nei, 1997, Molecular Biol. Evol. 4:406-425) was computed. The gene tree was generated using
5 homologous genes identified with a BLASTP search against NCBI non-redundant database, using the human EST AA481214 sequence as a query. The resulting tree indicates that the identified human EST AA481214 represents a true ortholog of the *C.elegans* gene gi|1132541 (Figure 14B). The nucleotide sequence of the death domain protein is shown in Figure 14C, as well as the deduced amino acid sequence
10 presented in Figure 14D.

6.1.2 APOPTOSIS GENE DISCOVERY METHOD

As a first step in identifying a novel gene involved in apoptosis, a comprehensive set of articles describing the system of apoptosis/programmed cell
15 death in different species was compiled using the keyword "apoptosis". By analyzing the articles, information on regulatory pathways characterizing this system in different species, *i.e.*, *C. elegans*, mouse, fruit fly, chicken, and human, was extracted. The regulatory information was stored as a collection of schemes produced in PowerPoint (Microsoft). Figure 4 shows a set of keywords defining proteins involved in apoptosis
20 pathways. The keywords were used to generate a specialized sequence database, referred to as Apoptosis3, utilizing the PsiRetriever program for extraction of proteins from the all-inclusive non-redundant GenBank database (NCBI). Using program PsiRetriever, sequences from the non-redundant (NCBI) database of protein sequences, were retrieved and stored as a FASTA file. The FASTA file was then
25 converted into binary blast database using program FORMATDB from the BLAST suit of programs.

Genomic and cDNA sequences located in the region of human chromosome 13q were compared with the Apoptosis3 database using BLASTALL program from BLAST program complex. This region of the human genome is
30 associated with Chronic Lymphocytic Leukemia (CLL). The comparison revealed significant similarity between a CLL region open reading frame and the mouse RPT1

protein (sp|P15533|RPT1) (Figure 13). Analysis of regulatory functions of RPT1 in the mouse reveals that this gene functions as a repressor of the interleukin 2 receptor (IL-2R) gene. When the RPT1 gene is knocked out, the regulatory effect is manifested as a block of the apoptotic pathway in T lymphocytes resulting in an accumulation of T lymphocytes in blood. This result is consistent with aberrations observed in CLL, namely abnormal accumulation of B-cells in the blood (Trentin L. et al., 1997, Leuk. Lymphoma 27:35-42) and mutations in the human RPT1 gene play a role in development of CLL.

6.1.3 EXAMPLE: A DISCOVERY OF A HUMAN ORTHOLOG OF THE MURINE MAX-INTERACTING TRANSCRIPTIONAL REPRESSOR

The family of *Myc* proto-oncogenes encodes a set of transcription factors implicated in regulation of cell proliferation, differentiation, transformation and apoptosis. C-*Myc* null mutations result in retarded growth and development of mouse embryos and are lethal by 9-10 day of gestation. In contrast, overexpression of *Myc* genes inhibits cell differentiation and leads to neoplastic transformation. Moreover, deregulation of *Myc* expression by retroviral transduction, chromosomal translocation or gene amplification is linked to a broad range of naturally occurring tumors in humans and other species.

Another protein, called *Max*, is an obligatory heterodimeric partner for *Myc* proteins in mediating their function as activators of transcription during cell cycle progression, neoplastic transformation and programmed cell death (apoptosis). In order to make an active transcription factor the *Myc* proteins must form heterodimers with *Max* protein. This interaction with *Max* protein is necessary for specific binding of *Myc* with CACGTG box (or related E-boxes) on DNA and for activation of promoters located proximal to the binding sites.

Besides the *Myc* family of transcription factors, the *Max* protein forms complexes with another family of so-called *MAD* proteins: *Mxi1*, *MAD1*, *MAD3* and *MAD4*. Whereas *Myc:Max* complexes activate transcription, *MAD:Max* complexes work in an opposite way repressing the transcription through the same E-box binding

sites and apparently antagonize *Myc*-mediated activation of the same set of target genes.

During tissue development a shift from *Myc:Max* to *MAD:Max* complexes occurs coincidentally with the switch from cell proliferation to differentiation. The switch in heterocomplexes is thought to reflect a switch from activation to repression of common genes leading to cessation of proliferation, exiting the cell cycle and the beginning of cell differentiation. In differentiating neurons, primary keratinocytes, myeloid cell lines and probably other tissues the expression of different *MAD:Max* complexes appear in sequential order during the transition from cell proliferation to differentiation. The *MAD3* expression appears first and it is restricted to proliferating cells prior to differentiation where it is co-expressed with two different member of *Myc* family, c-*Myc* or N-*Myc*. *Mxi1* transcripts are detected in proliferating and differentiating cells whereas *MAD1* and *MAD4* were confined to post-mitotic cells. Because *Myc* expression is not always downregulated in post-mitotic cells, co-expression of *Myc* and *MAD* genes may result in competition for *Max* heterodimers thus providing promoting or inhibitory effect on cell proliferation.

The gene expression patterns, along with ability of Mad proteins to suppress *Myc*-dependent transformation, are consistent with a potential function of Mad genes as tumor suppressors. This view is supported by the fact that allelic loss and mutations were detected at the *Mxi1* locus in prostate cancers (Eagle et al., 1995 Nat Genet 9:249-55). Cloning of the murine proteins *Mad3* and *Mad4* as well as their relation to *Max* signaling network was described by Hurlin (Hurlin PJ, et al., 1995, EMBO J. 14:5646-59) and Queva (Queva et al. 1998 Oncogene 16:967-977). Human orthologs of *Mad4*, *Mad1* and *Mxi1* are known.

In this example, the discovery of an unknown human ortholog of *Mad3* protein found "*in silico*," by means of phylogenetic analysis of known mouse and human members of the *Mad* gene family and database searches is described. Since the function of murine *Mad3* as a *Max*-interacting transcriptional repressor of *Myc*-induced neoplastic transformation is well described, we can assign the same function to its human ortholog.

The gene tree shown in the Figure 20 was constructed in the following way. The protein sequences of known members of *Mad* gene family were extracted from GenBank database using NCBI Entrez keyword searches. The extracted sequences were aligned using multiple alignment program Clustalw running on Sun SPARC station. The quality of the multiple alignment was checked using program HitViewer Iterate (A. Rzhetsky, available upon request) and the redundant, non-homologous sequences as well as distant homologs from *S. cerevisiae*, *C. elegans*, *D. melanogaster* etc. were removed from the alignment. The refined set of sequences was realigned with Clustalw and a gene tree as presented in Figure 15A was computed from the alignment using program NJBOOT ([http://genome6.cpmc.columbia.edu // andrey](http://genome6.cpmc.columbia.edu//andrey)) running on Sun SPARC station and viewed with program TreeView ([http://genome6.cpmc.columbia.edu // andrey](http://genome6.cpmc.columbia.edu//andrey)).

The tree presented in Fig.19A clearly shows the relationships between three known mouse genes and their two human homologs. Attempts to find a missing human ortholog of the mouse *Mad3* gene in protein non-redundant database at NCBI using BLAST search did not identify any human homologs other than sequences that were already present on the tree, confirming the absence of a known human ortholog for Mad3 protein in the database.

In order to identify a human ortholog of the Mad3 protein, a human dbEST at NCBI was searched with program TBLASTN using Mad3 protein sequence as a query. Two EST were identified and are shown in Figure 17A.

Due to the nature of dbEST database this search produced only partial sequences of potential candidate genes. To obtain complete coding sequences (complete cds) of the genes, a search was conducted to obtain overlapping sequences in dbEST. The search for overlapping sequences was performed using the program Iterate with EST zs77e55.r1 (gb|AA278224) serving as a query. The search returned a single overlapping sequence, namely HUMGS0012279 (dbj|C02407), thus indicating that the two EST sequences found during the initial TBLASTN search belong to the same gene.

The complete sequence of the gene was assembled from the two ESTs using commercially available sequence assembly program SeqManII (DNASTAR Inc.,

WI). The nucleotide sequence of the human *Mad3* gene is presented in Figure 17B. The deduced amino acid sequence of the gene is presented in Figure 17C. The translated sequence consists of 206 amino acid residues 81% of which are identical to mouse Mad3 protein. The alignment of human and mouse Mad3 proteins shown below was made using
5 BLAST server at NCBI and is presented in Figure 17C.

Multiple alignment of the new sequence with sequences of known Mad proteins was made using Clustalw and viewed with the HitViewer. A gene tree was computed from this alignment using NJBOOT. Multiple alignment of the new sequence with sequences of known Mad proteins (Figure 17C) along with its position
10 on gene tree (Figure 18B) shows that this new human gene found by the approach described above belongs to the family of Mad proteins and is the ortholog of mouse Mad3.

The present invention is not to be limited in scope by the specific embodiments described herein, which are intended as single illustrations of individual
15 aspects of the invention, and functionally equivalent methods and components are within the scope of the invention. Indeed, various modifications of the invention, in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and accompanying drawings. Such modifications are intended to fall within the scope of the appended claims.

20 Various publications are cited herein, the contents of which are hereby incorporated by reference in their entireties.

CLAIMS

1. A method for identifying a novel nucleic acid molecule encoding a protein of interest comprising:
- 5 (i) selecting a specific protein from a first species involved in a regulatory network of interest;
- (ii) identifying known proteins that act upstream and downstream in the regulatory network of interest with respect to the specific protein selected;
- 10 (iii) constructing the regulatory network of interest from the proteins identified in step (ii);
- (iv) for each identified protein, select a domain or motif and search by homology for related proteins in a second species, wherein a related protein is defined as a protein having a homologous domain or motif;
- 15 (v) producing a regulatory network for the second species, wherein said regulatory network incorporates the identified related proteins;
- (vi) comparing the regulatory network from the first species to the regulatory network of said second species;
- 20 (v) identifying a protein present in a regulatory network for one species but absent in the regulatory network of the other species; and
- (vi) isolating a nucleic acid molecule encoding the protein identified in step (v) in the species in which it is missing.
- 25 2. The method of Claim 1 wherein the nucleic acid molecule encodes human protein.
3. The method of claim 1 wherein the related proteins are orthologs.

4. The method of claim 1 wherein the regulatory pathway is involved in apoptosis.
5. The method of claim 1 wherein the specific protein from the first species is involved in tumor suppression.
6. A method for identifying the affect of a gene knockout on a regulatory pathway comprising the following steps:
 - (i) identification of the shortest non-oriented pathway connecting two gene products;
 - 10 (ii) assigning an initial sign value of "-" to the knockout since the knockout gene product is inactive;
 - (iii) moving along the shortest pathway between the two gene products multiplying the sign with the sign of the next gene product in the pathway, wherein "-" stands for inhibition, "+" stands for induction or activation, and "0" stands for the lack of interaction between two proteins in the specified direction; and
 - 15 (iv) determining the final sign at the end of the pathway, wherein "-" indicates inhibition and "+" indicates induction or activation of the pathway.
- 20 7. A method for identifying a novel nucleic acid molecule encoding a protein of interest comprising:
 - (i) selecting a gene of interest and searching a database for homologous sequences;
 - 25 (ii) aligning the homologous sequences identified in step (i);
 - (iii) constructing a gene tree using the sequence alignment;
 - (iv) constructing a species tree;

- 5 (v) imputing the species tree and gene tree into an algorithm which integrates the species tree and the gene tree into a reconciled tree; and
- (vi) identifying orthologous genes present in one species but missing in another.

8. The method of claim 7 wherein the following algorithm is used to integrate the species tree and the gene tree into a reconciled tree:

- 10 (i) computing the similarity $\sigma(S_{gi}, S_{sj})$ for each pair of interior nodes from trees T_g and T_s ,
- (ii) finding the maximum $\sigma(S_{gi}, S_{sj})$;
- (iii) saving S_{gi} as a new cluster of orthologs, save $\{S_{gi}\} - \{S_{sj}\}$ as a set of species that are likely to have gene of this kind (or lost it in evolution);
- (iv) eliminating S_{gi} from T_g ; $T_g := T_g \setminus S_{gi}$;
- 15 (v) repeating step (ii)-(iv) until T_g is non-empty.

9. A method for identifying a novel gene comprising the following steps:

- 20 (i) defining a motif or domain composition of a gene of interest;
- (ii) searching for sequences which correspond to nucleotide sequences in an expression sequence tag database or other cDNA databases using a program such as BLAST and retrieving the identified sequences;
- 25 (iii) searching additional databases for expressed sequence tags containing the domains and motifs characteristic for the gene of interest with Hidden Markov Model of domains and motifs identified in step (i);
- (iv) identifying nucleotide sequences comprising the gene of interest.

10. The method of claim 9 further comprising using each identified expression sequence tag to search sequence databases for overlapping sequences for the purpose of assembling longer overlapping stretches of DNA.
- 5
11. A method for extracting information on interactions between biological entities from natural-language text data, comprising:
- (i) parsing the text data to determine the grammatical structure of the text data ;and
 - 10 (ii) regularizing the parsed text data to form structured word terms.
12. The method according to claim 11, further comprising preprocessing the data prior to parsing, with preprocessing comprising the step of identifying biological entities.
13. The method according to claim 11, further comprising referring
15 to an additional parameter which is indicative of the degree to which subphrase parsing is to be carried out.
14. The method according to claim 11, wherein said parsing step further comprises segmenting the text data by sentences.
15. The method according to claim 11, wherein said parsing step
20 further comprises:
- segmenting the text data by sentences; and
 - segmenting each of the sentences at identified words or phrases.
16. The method according to claim 11, wherein said parsing step further comprises:
- 25
- segmenting the text data by sentences; and
 - segmenting each of the sentences at a prefix.

17. The method according to claim 11, wherein said parsing step further comprises skipping undefined words.

18. The method according to claim 11, wherein said parsing step further comprises:

- 5 identifying one or more binary actions and their relationships; and
identifying one or more arguments associated with the actions.

19. The method according to claim 11, further comprising performing error recovery when parsing of the text data is unsuccessful.

20. The method according to claim 19, wherein said error recovery
10 step comprises:
segmenting the text data; and
analyzing the segmented text data to achieve at least a partial parsing of
the unsuccessfully parsed text data.

21. The method according to claim 11, wherein said tagging step
15 comprises providing the structured data component in a Standard Generalized Markup
Language (SGML) compatible format.

22. A computer system for extracting information on biological entities from natural-language text data, comprising:

- (i) means for parsing the natural-language text data; and
20 (ii) means for regularizing the parsed text data to form structured
word terms.

23. The system according to claim 22, further comprising means for preprocessing the data prior to parsing, with the preprocessing means comprising
25 identifying biological entities.

24. The system according to claim 22, further comprising means for referring to an additional parameter which is indicative of the degree to which subphrase parsing is to be carried out.

25. The system according to claim 22, wherein said parsing means
5 further comprises means for segmenting the text data by sentences.

26. The system according to claim 22, wherein said parsing means further comprises:
means for segmenting the text data by sentences; and
means for segmenting each of the sentences at identified words or
10 phrases.

27. The system according to claim 22, wherein said parsing means further comprises:
means for segmenting the text data by sentences; and
means for segmenting each of the sentences at a prefix.

15 28. The system according to claim 22, wherein said parsing means further comprises means for skipping undefined words.

29. The system according to claim 22, wherein said parsing means further comprises:
means for identifying one or more binary actions and their relationships;
20 and
means for identifying one or more arguments associated with the actions.

30. The system according to claim 22, further comprising means for performing error recovery when parsing of the text data is unsuccessful.

31. The system according to claim 22, wherein said error recovery means comprises:

means for segmenting the text data; and

5 means for analyzing the segmented text data to achieve at least a partial parsing of the unsuccessfully parsed text data.

32. The system according to claim 22, wherein said tagging means comprises means for providing the structured data component in a Standard Generalized Markup Language (SGML) compatible format.

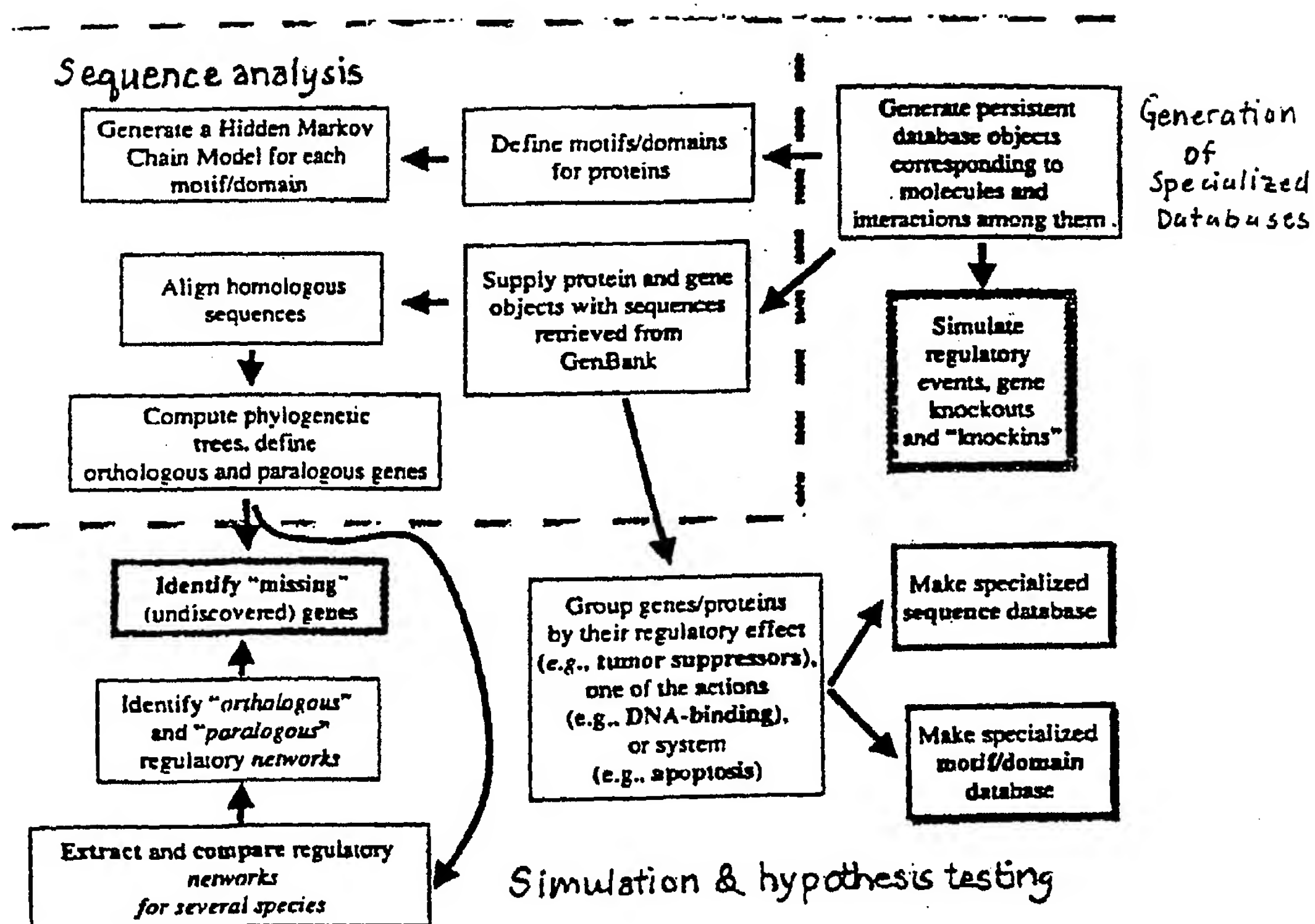


FIGURE 1

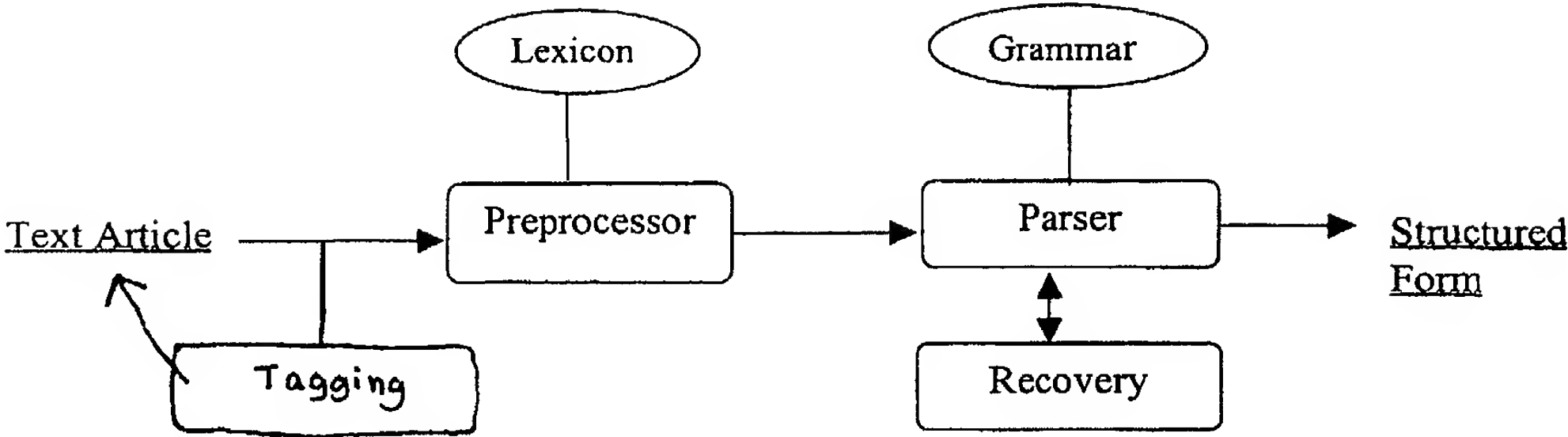


Figure 2

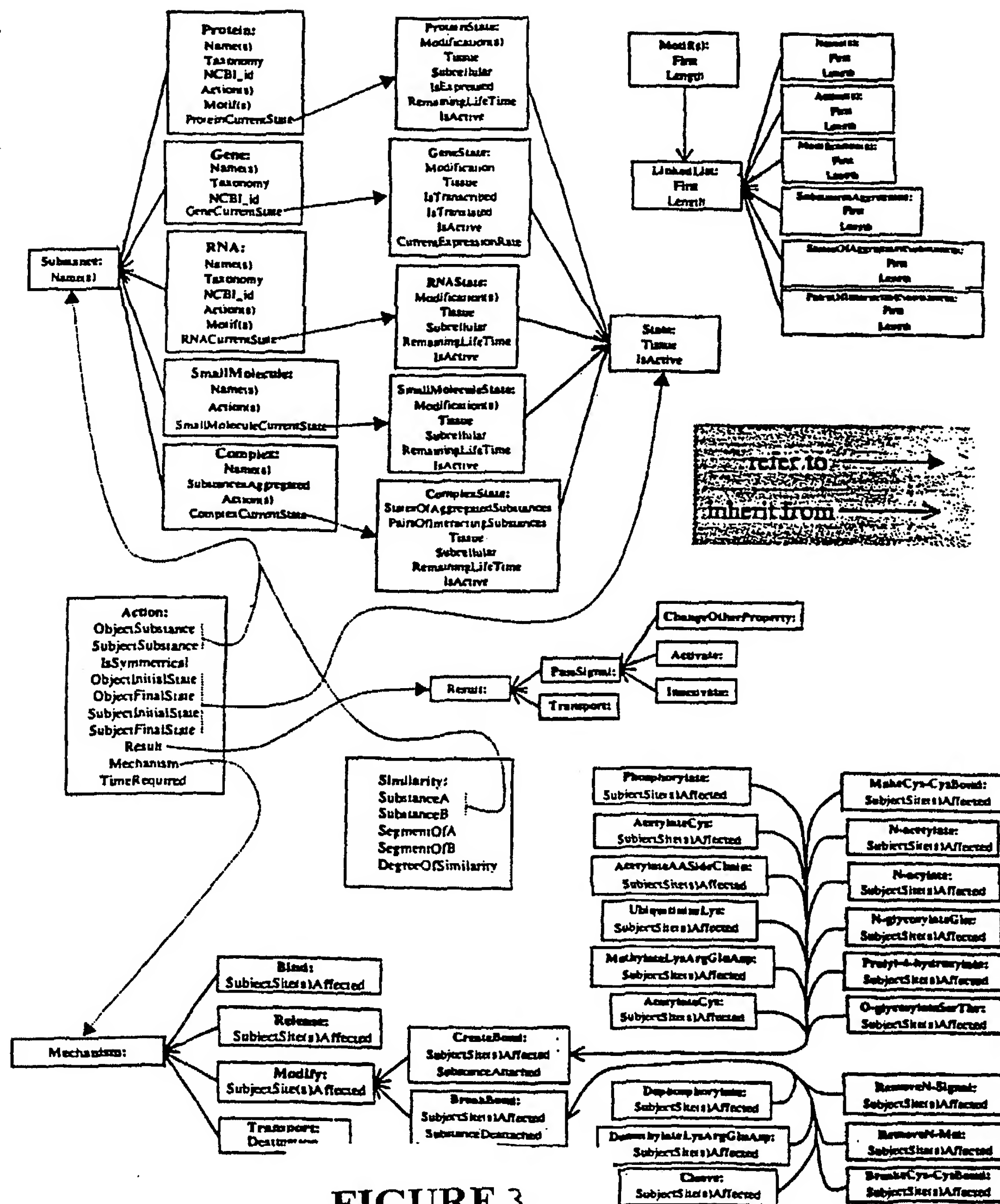


FIGURE 3

FIGURE 4

bcl-xL / bcl / bcl-xS / ccd-9 / Bax / Btk / Bak / p21 / NGF1-B / N10 / Nak1 / Nur77 / Nur71 / Nur1 / Not-1 / RXR / galectin-1 / N-glycan / CNTF / lck / fyn / ZAP-70 / raf / ras / MAP / protein kinase C / PKC / phosphatase calcineurin / NF-AT / AP1 / 14-3-3 / Raf-1 / Bcl-2 / Interleukin / IL-1 / IL-3 / cytokine / IGF-1 / CD95 / Apo-1 / RIP / FAF1 / FADD / FAP-1 / TNFR / TRAF / TRAP1 / TRAP2 / TRADD / HIAP1 / HIAP2 / CD40 / CD30 / XIAP / CD2 / CD3 / TCR / Bcl-w / Mcl-1 / NR-13 / BHRF1 / HMWS-HL / E1B19K / Nbk / Mch2 / CPP32 / ICE / FLICE / Nedd-2 / TX / Mch3 / Mch4 / ICH-1s / nuc-1 / DNase1 / caspase / MACH1 / Mch5 / apopain / Yama / ICH / CMH / ccd-3 / ccd-4 / ccd-9 / p53 / MKK3 / MKK1 / MEK2 / MKK4 / BAG-1 / Src / FAK / p38 / p42 / ERK1 / p44 / ERK2 / SAPK / JNK / MEK / C-JUN / MEF2D / ATF2 / calcineurin / ELK-1 / protein phosphatase 2A / raf-1 / IL-1 beta / TNF / PTK / Apaf / p35 / ETS / C-Myc / IL-2 / IL-2 receptor / NF-kappa B / TNFR-1 / TRAIL / Apo-2L / DR4 / death receptor / DR3 / DR2 / DR5 / DR1 / bad / BMPR / BMP-x / TGF / grim / hid / FAN / perforin / Fas-L / Fas / DcR1 / decoy receptor / wsl-1 / NGF receptor / growth factor / RAR

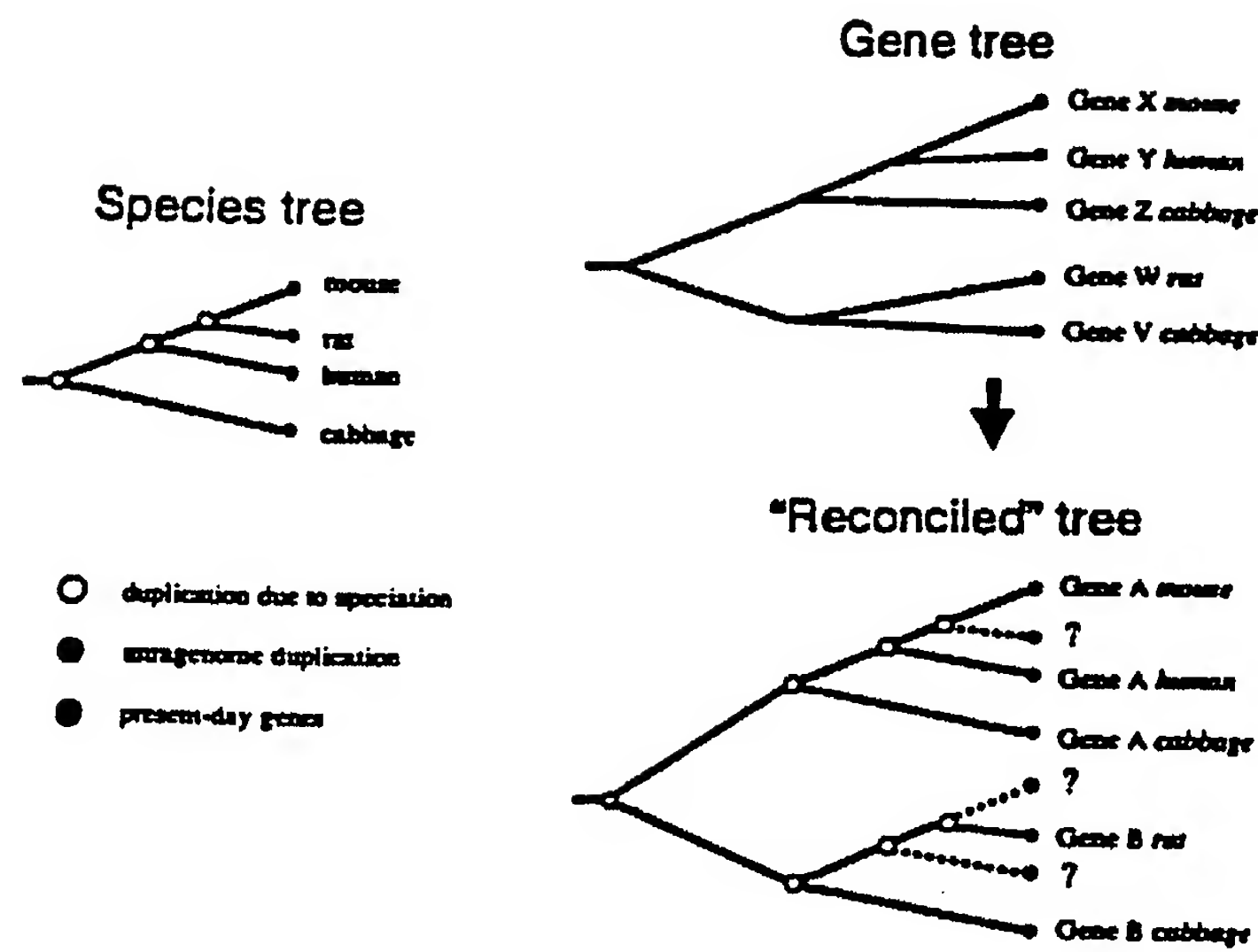


FIGURE 5

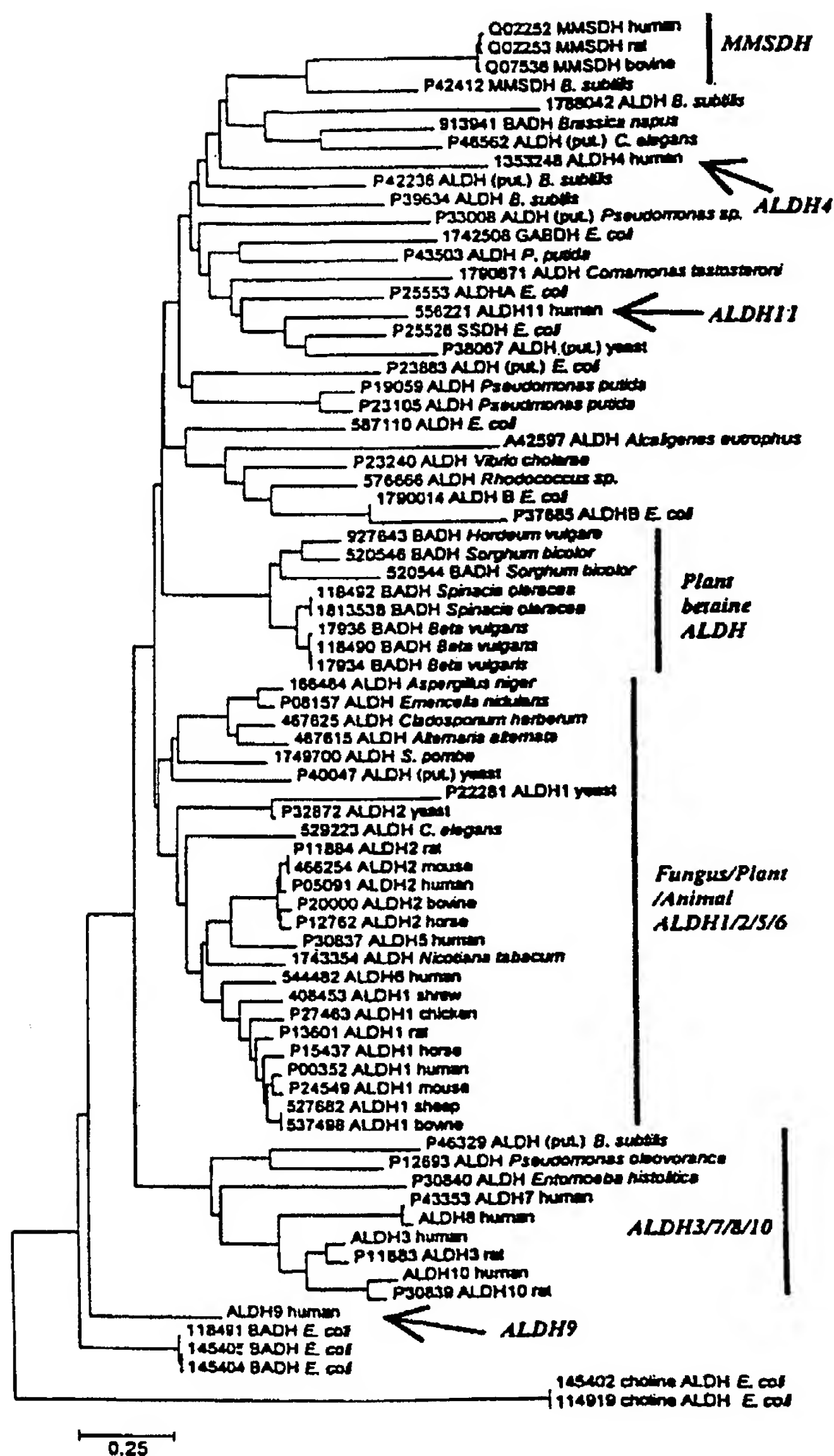


FIGURE 6

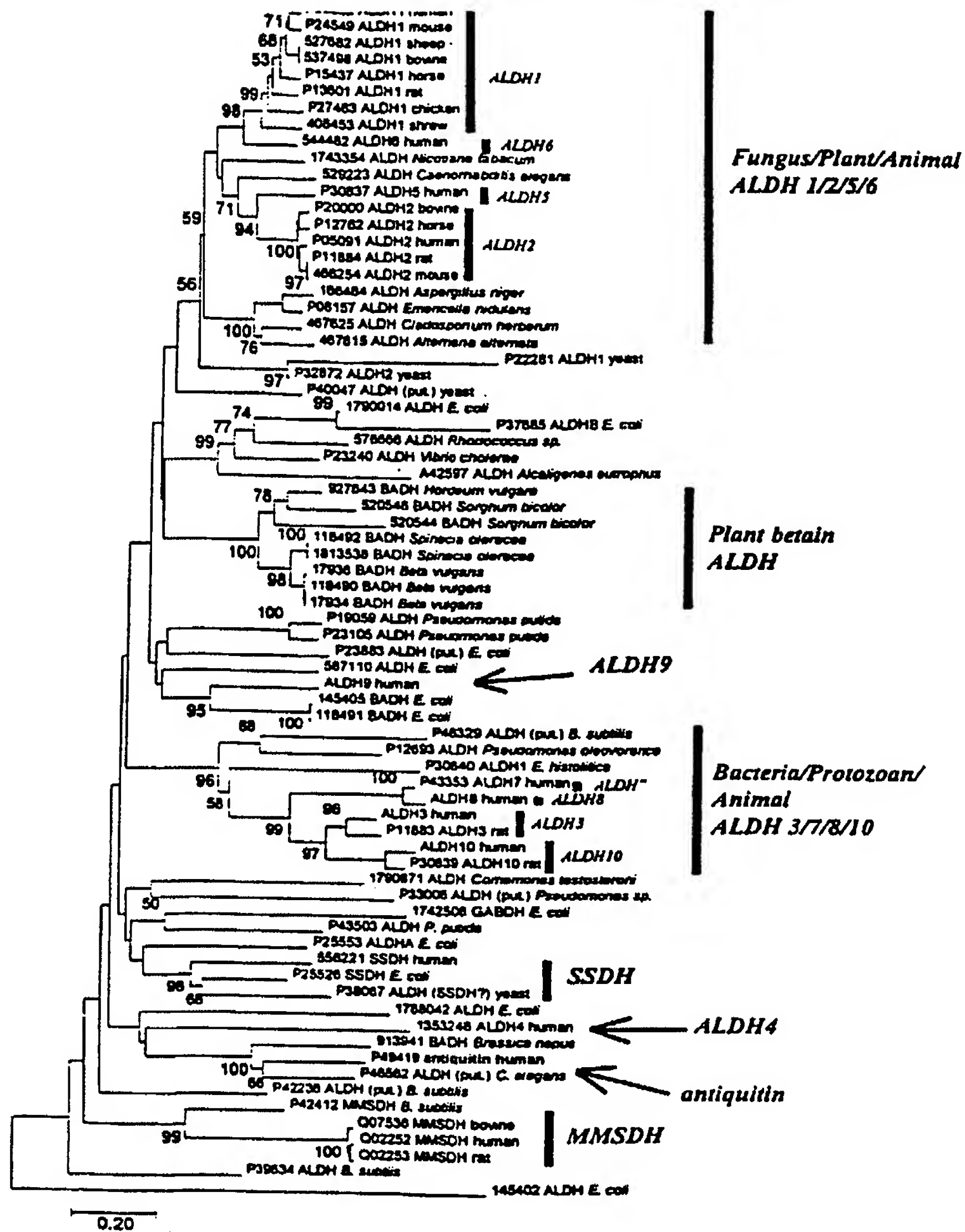
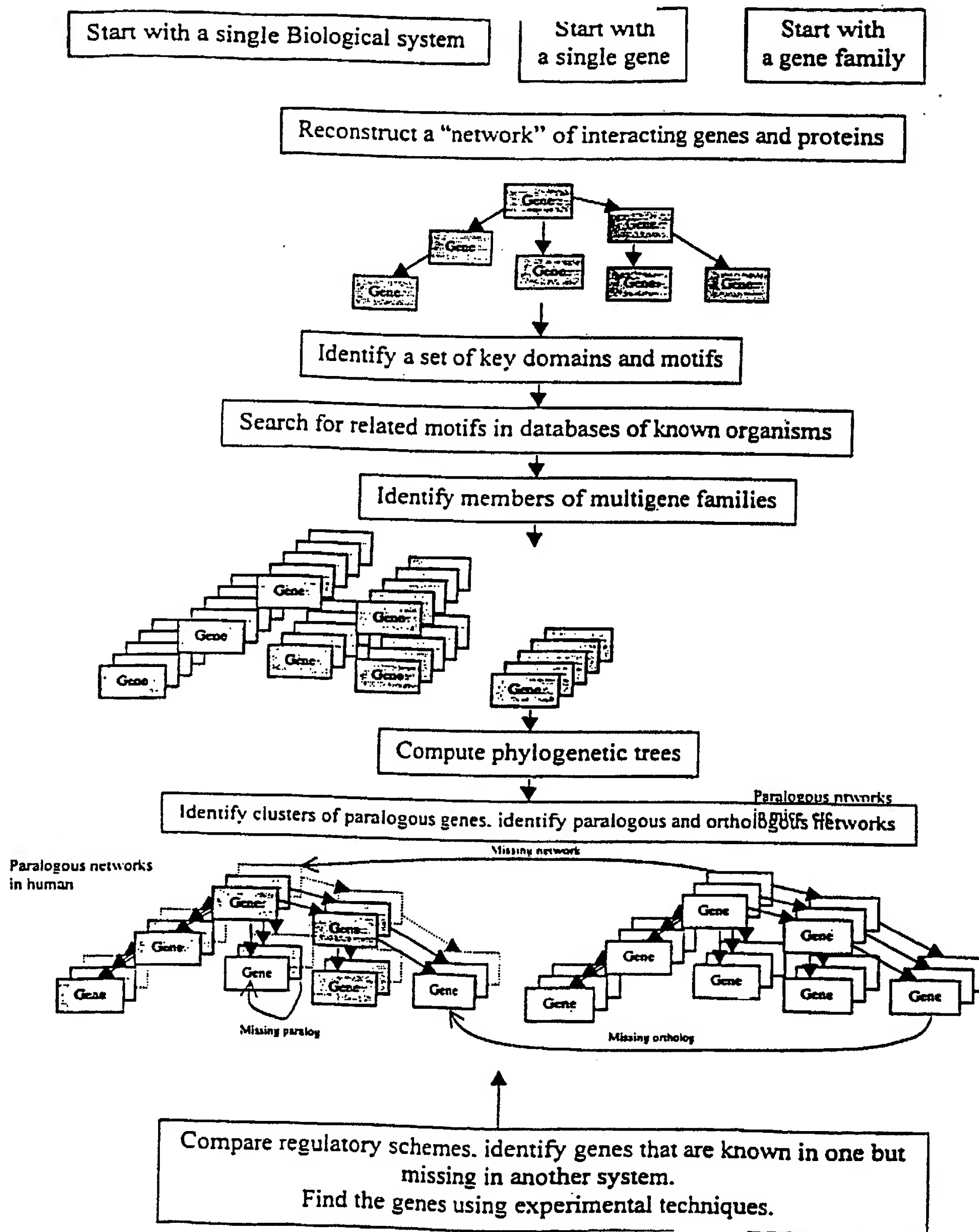


FIGURE 7

FIGURE 8

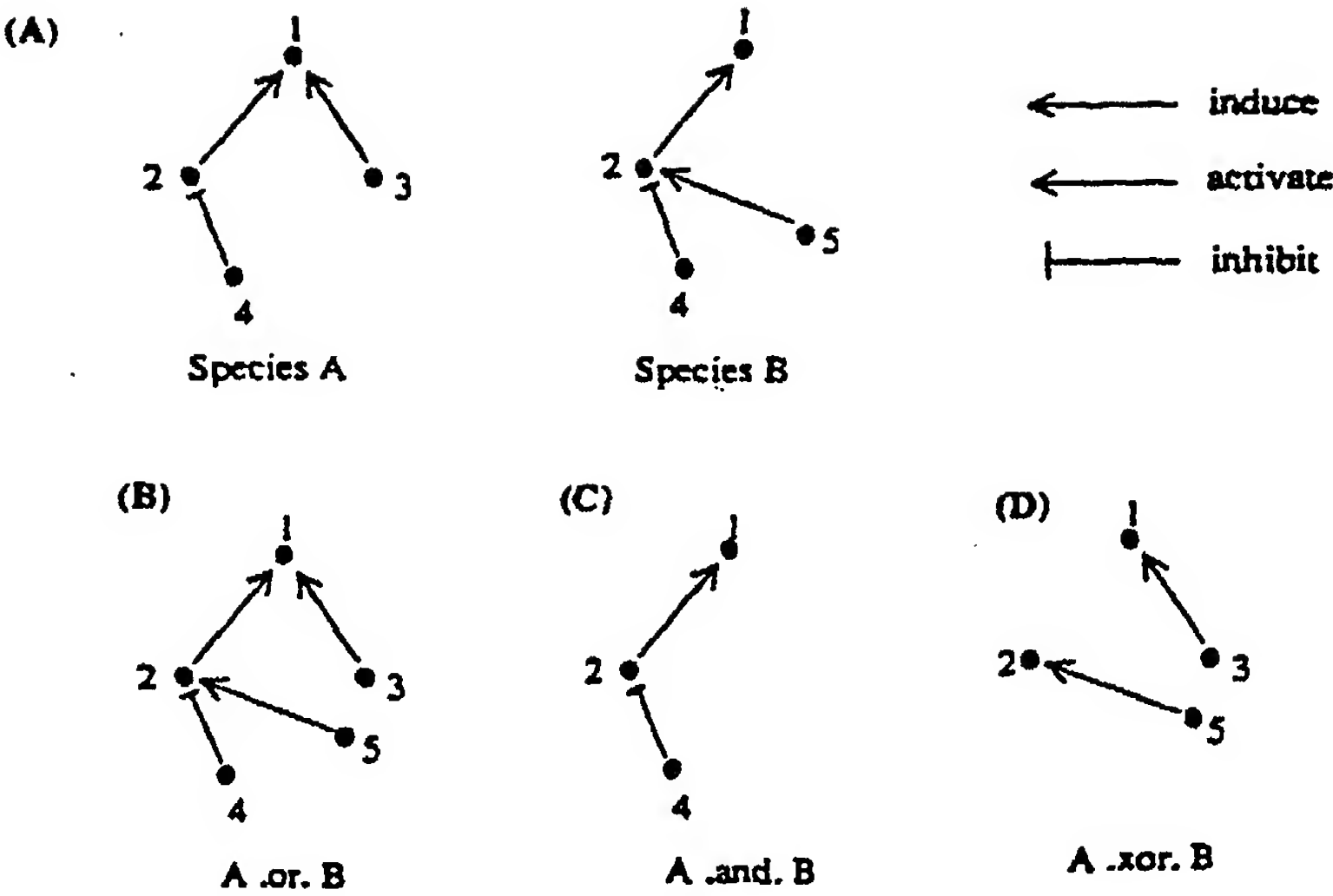


FIGURE 9

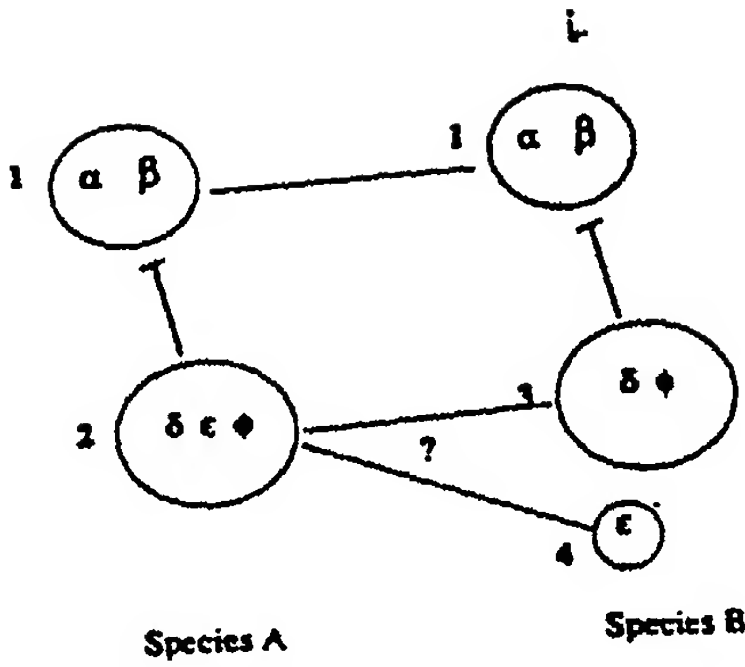


FIGURE 10

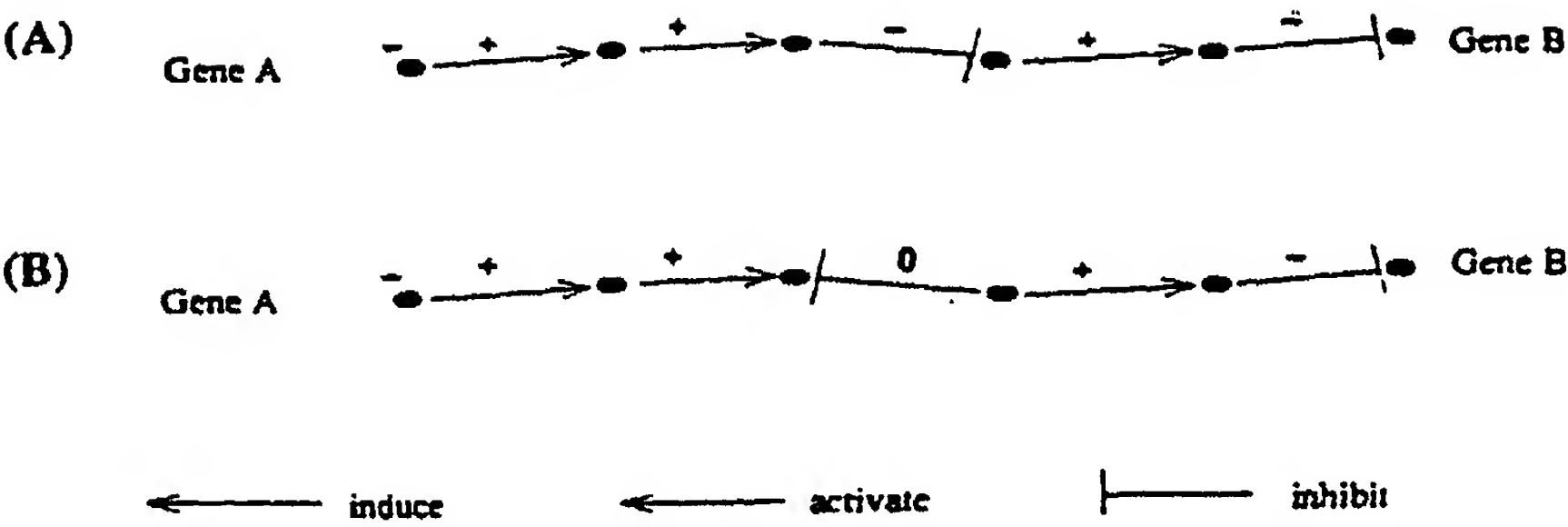


FIGURE 11

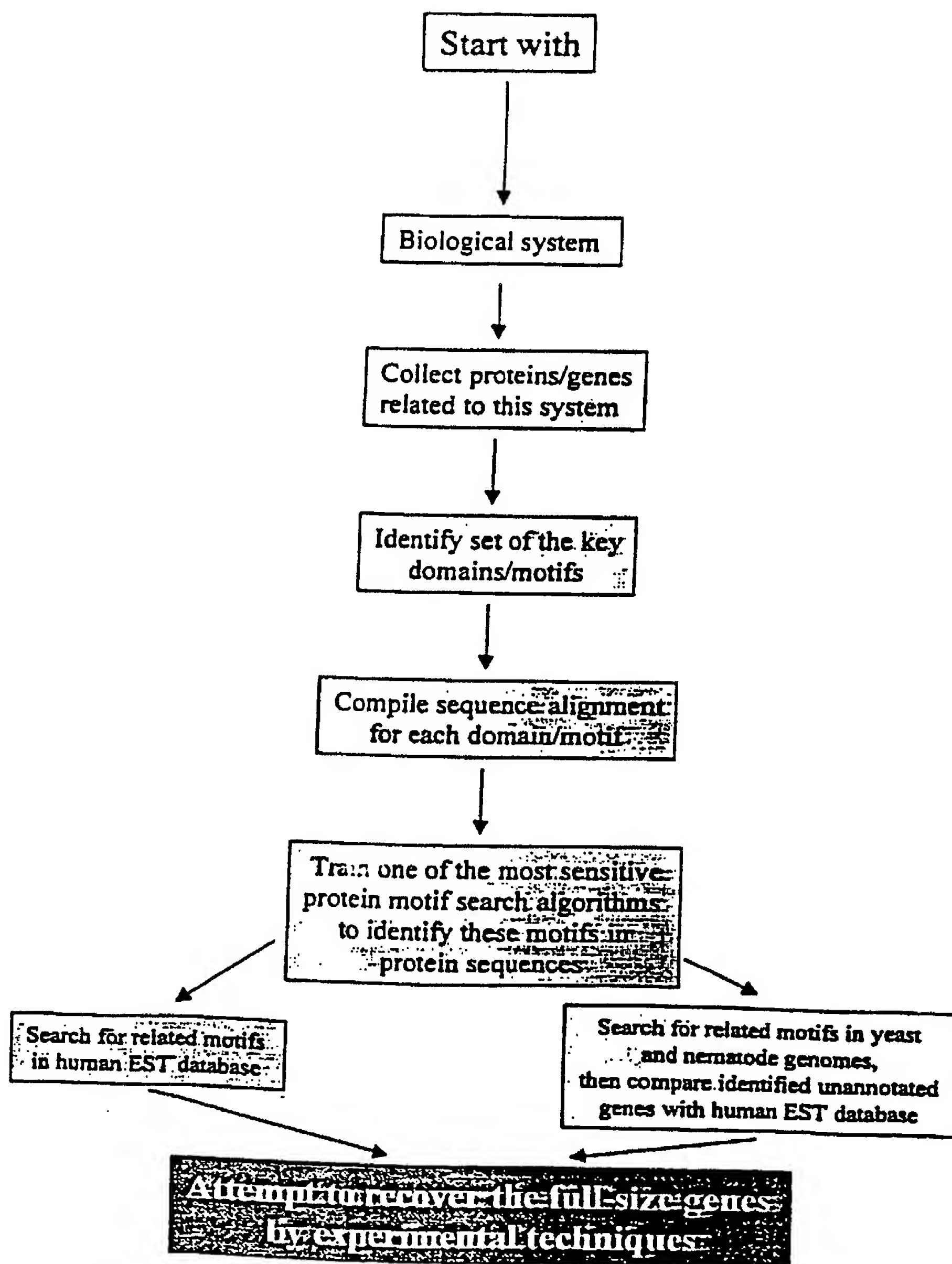


FIGURE 12

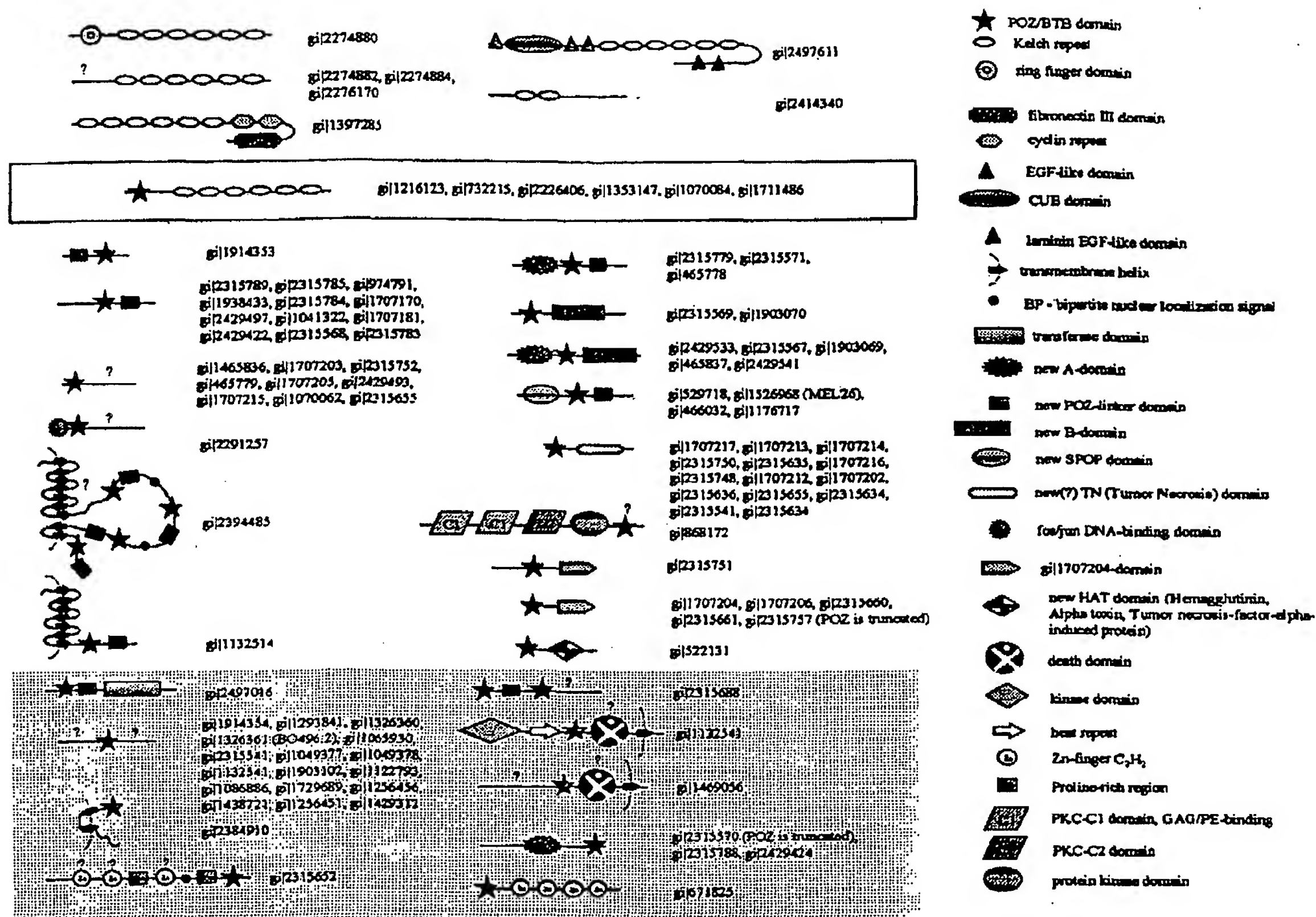


Figure 13

>gi|2210766|gb|AA481214|AA481214 aa34e02.r1 NCI_CGAP_GCB1 Homo sapiens cDNA clone
IMAGE:815162 5' similar to WP:W07A12.4 CE03795 ;, mRNA sequence [Homo sapiens]
CATGGCTTCCTGGACACCAACCCTGCCATCCGGGAGCAGACGGTCAAGTCCATGCTGCTCCTGGCCCCAA
AGCTGAACGAGGCCAACCTCAATGTGGAGCTGATGAAGCACTTTGCACGGCTACAGGCCAAGGATGAACA
GGGCCCCATCCGCTGCAACACCACAGTCTGCCTGGGCAAAATCGGCTCCTACCTCAGTGCTAGCAACCAGA
CACAGGGTCCTTACCTCTGCCTTCAGCCGAGCCACTAGGGACCCGTTTGACCCGTCCCGGGTTGCGGGTG
TCCTGGGCTTTGCTGCCACCCACAACCTCTACTCAATGAACGACTGTGCCCAGAAGATCCTGCCTGTGCT
CTGCGGTCTCACTGTAGATCCTGAGAAATCCGTGCGAGACCAGGCCTTCAAGGCA

>gi|1349211|gb|W51957|W51957 zc45f01.r1 Soares_senescent_fibroblasts_NbHSF Homo
sapiens cDNA clone IMAGE:325273 5', mRNA sequence [Homo sapiens]
CCTTCGAGTTCGGCAATGCTGGGGCCGTTGTCTCAGCCCCCTCTTCAAGGTGGGCAAGTTCCTGAGCGC
TGAGGAGTATCAGCAGAAGATCATCCCTGTGGTGGTCAAGATGTTCTCATCCACTGACCGGGCCATGCGC
ATCCGNCTCCTGCAGCAGATGGAGCAGTTCATCCAGTACCTTGACGAGCCACAGTCAACACCCAGATCT
TCCCCACGTCTGTACATGGCTTCCTGGACACCAACCCTGCCATCCGGGAGCAGACGGTCAAGTCCATGCT
GCTCCTGGCCCCAAAGCTGAACGAGGCCAACCTCAATGTGGAGCTGATGAAGCACTTTGCACGGCTACAG
GCCAAGGATGAACAGGGCCCCATCCGCTGCAACACCACAGTCTGCCTGGGCAAAATCGGCTCCTACCTCA
GTGCTAGCACCAGACACAGGGTCCTTACCTCTG

Figure 14 A

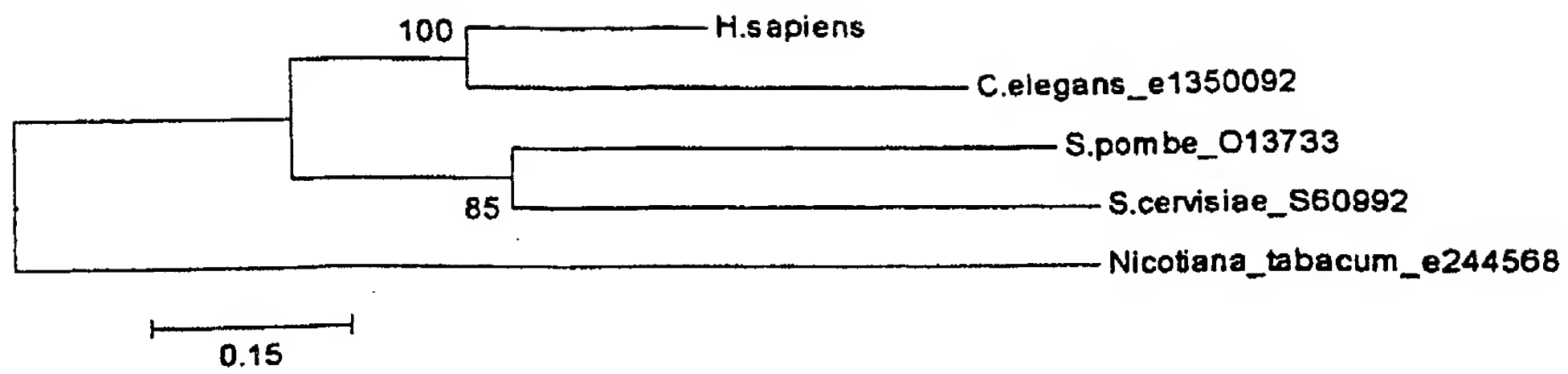


Figure 14B

BASE COUNT	405 a	545 c	493 g	278 t	6 others	
ORIGIN						
1	cagccgaagc	amgcaaaaat	tcttccagga	gctgagcaag	agcctggacg	cattccctga
61	ggayttctgt	cggcacaagg	tgctgcccc	gctgctgacc	gccttcgagt	tcggcaatgc
121	tggggccggt	gtcctcacgc	ccctcttcaa	ggtgggcaag	ttcctgagcg	ctgaggagta
181	tcagcagaag	atcatccctg	tggtggtcaa	gatgtttctca	tccactgacc	gggccatgcg
241	catccgcctc	ctgcagcaga	tggagcagtt	catccagtac	cttgacgagc	caacagtcaa
301	caccagatc	ttccccacg	tcgtacatgg	cttcctggac	accaaccctg	ccatccggga
361	gcagacggtc	aagtccatgc	tgctcctggc	cccaaagctg	aacgaggcca	acctcaatgt
421	ggagctgatg	aagcactttg	cacggctaca	ggccaaggat	gaacagggcc	ccatccgctg
481	caacaccaca	gtctgcctgg	gcāaaatcgg	ctcctacctc	agtgtctagca	ccagacacag
541	ggtcettacc	tctgccttca	gccgagccac	tagggaccog	tttgaccggt	ccggggttgc
601	gggtgtcctg	ggctttgctg	ccaccacaa	cctctactca	atgaacgact	gtgccagaa
661	gacctgcct	gtgctctgcg	gtctcactgt	agatcctgag	aaatccgtgc	gagaccaggc
721	cttcaaggcm	wttcggagct	tcctgtccaa	attggagtct	gtgtcggagg	acccgaccca
781	gctggaggaa	gtggagaagg	atgtccatgc	agcctccagc	cctggcatgg	gaggagccgc
841	agctagctgg	gcaggctggg	cgtgaccogg	gtctcctcac	tcacctccaa	gctgatccgt
901	tcgcacccaa	ccactgcccc	aacagaaacc	aacattcccc	aaagacccac	gcctgaagga
961	gttcctgccc	cagccccccac	ccctgttcct	gccaccccta	caacctcagg	ccactgggag
1021	acgcaggagg	aggacaagga	cacagcagag	gacagcagca	ctgctgacag	atgggacgac
1081	gaagactggg	gcagcctgga	gcaggaggcc	gagtctgtgc	tggcccagca	ggacgactgg
1141	agcaccgggg	gccaaagtga	ccgtgctagt	caggtcagca	actccgacca	caaatectcc
1201	aaatccccag	agtccgactg	gagcagctgg	gaarctgagg	gctcctggga	acagggctgg
1261	caggagccaa	gctcccagga	gccacctyct	gacggtacac	ggctggccag	cgagtataac
1321	tggggtggcc	cagagtccag	cgacaagggc	gaccccttcg	ctaccctgtc	tgacgtccc
1381	agcaccagc	cgaggccaga	ctcttggggt	gaggacaact	gggagggcct	cgagactgac
1441	agtcgacagg	tcaaggctga	gctggccccg	aagaagcgcg	aggagcggcg	gcgggagatg
1501	gaggccaaac	gcgcccagag	gaagggtgcca	agggccccat	gaagctggga	gcccggaagc
1561	tggactgaac	cgtggcggtg	gcccttcccg	gctgcggaga	gcccgcccca	cagatgtatt
1621	tattgtacaa	accatgtgag	cccggccgcc	cagccaggcc	atctcacgtg	tacataatca
1681	gagccacaat	aaattctatt	tcacaaaaaa	aaaaaaaaaa	aaaaaaa	

//

Figure 14C

	5	10	15	20	25	30																								
1	S	R	S	X	Q	K	F	F	Q	E	L	S	K	S	L	D	A	F	P	E	D	F	C	R	H	K	V	L	P	Q
31	L	L	T	A	F	E	F	G	N	A	G	A	V	V	L	T	P	L	F	K	V	G	K	F	L	S	A	E	E	Y
61	Q	Q	K	I	I	P	V	V	V	K	M	F	S	S	T	D	R	A	M	R	I	R	L	L	Q	Q	M	E	Q	F
91	I	Q	Y	L	D	E	P	T	V	N	T	Q	I	F	P	H	V	V	H	G	F	L	D	T	N	P	A	I	R	E
121	Q	T	V	K	S	M	L	L	L	A	P	K	L	N	E	A	N	L	N	V	E	L	M	K	H	F	A	R	L	Q
151	A	K	D	E	Q	G	P	I	R	C	N	T	T	V	C	L	G	K	I	G	S	Y	L	S	A	S	T	R	H	R
181	V	L	T	S	A	F	S	R	A	T	R	D	P	F	A	P	S	R	V	A	G	V	L	G	F	A	A	T	H	N
211	L	Y	S	M	N	D	C	A	Q	K	I	L	P	V	L	C	G	L	T	V	D	P	E	K	S	V	R	D	Q	A
241	F	K	A	X	R	S	F	L	S	K	L	E	S	V	S	E	D	P	T	Q	L	E	E	V	E	K	D	V	H	A
271	A	S	S	P	G	M	G	G	A	A	A	S	W	A	G	W	A													

Figure 14D

>sp|P15533|RPT1_MOUSE DOWN REGULATORY PROTEIN
OF INTERLEUKIN 2 RECEPTOR (J03776) rpt-1r [Mus
musculus] Length = 353

Score = 92.0 bits (237), Expect = 6e-20

Query 194 VMELLEEDLTCPICCSLFDDPRVLPCHNFCKKCLEGILEGSVRNSMWRPAPFKCPTCRK 373
V+E+++E++TCPIC L +P C+H+FC+ C+ E S RN+ CP CR
Sbjct 5 VLEMIKEEVTCPICLELLKEFVSADCNHSFCRACITLNYE-SNRNT---DGKGNCPCVCRV 60

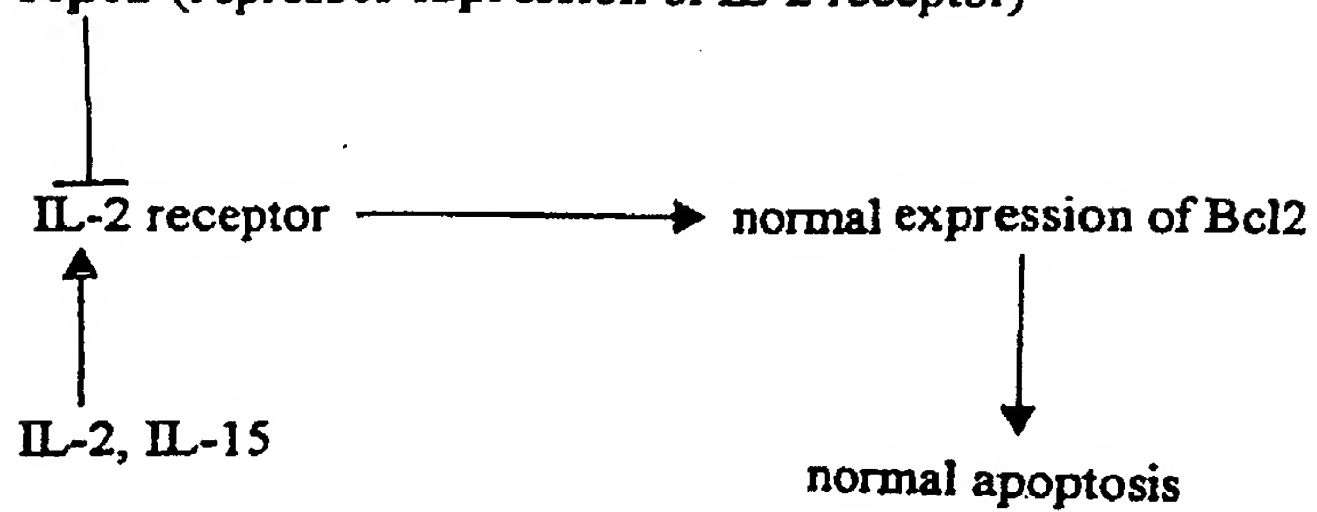
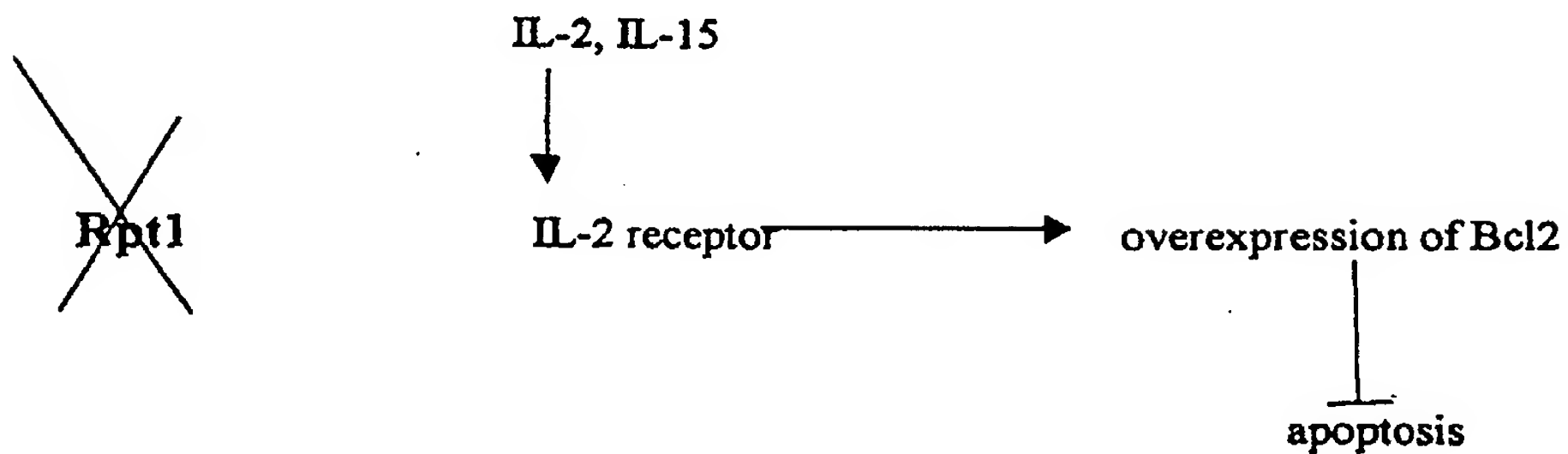
Query 374 ETSATGINSLOVNYSLKGIVEKYNKIKISP----KMPVCKGHMGQPLNIFCLTDMQLICG 541
+L+ N + IVE+ K P K+ +C H G+ L +FC DM +IC
Sbjct 61 PYP---FGNLRPNLHVANIVERLKGFKSIPEEEQKVNICAQH-GEKLRLFCRKMMVICW 116

Query 542 ICATRGEHTKHVFCSEIDAYAQERDAFESLFQSF-----ETWRRGDALSRLDTMETSK 700
+C EH H IE+ + ++ + + W+ L R+D
Sbjct 117 LCERSQEHGRGHQTALIEEVDQYKEKLOGALWKLMMKAKICDEWQDDLQQRVDW----- 171

Query 701 RKSLQLMTKDSDKVKEFFEKLQHTLDQKKNEILSDFETMKLAVMQAYDPEINKL 862
+Q+ + + V+ F+ L+ LD K+NE L + K VM+ + N+L
Sbjct 172 ENQIQI---NVENVQRQFKGLRDLDSKENEELQKLKKEKKEVMEKLEESENEL 222

Homology covers ring finger, B-box and the beginning of coiled coil domain
in the CLL ring finger protein

Figure 15

Activated CD4⁺ T-cells**Rpt1 (represses expression of IL-2 receptor)****When rpt1 is knocked out:****Figure 16**

TBLASTN 2.0.8 [Jan-05-1999]

Reference:

Altschul, Stephen F., Thomas L. Madden, Alejandro A. Schäffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997), "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res. 25:3389-3402.

Query= gi|2137498|Mad3m
(205 letters)

gb|AA278224|AA278224 zs77e05.r1 NCI_CGAP_GCB1 Homo sapiens cDNA clone IMAGE:703520 5'
similar to TR:G1184157 G1184157 MAX-INTERACTING
TRANSCRIPTIONAL REPRESSOR. ;
Length = 430

Score = 209 bits (526), Expect = 1e-53
Identities = 104/124 (83%), Positives = 116/124 (92%), Gaps = 1/124 (0%)
Frame = +2

Query: 1 MEPVASNIQVLLQAAEFLERREREAEHGYASLCPHHSPGTVCRRRKPPLOAPGALNSGRS 60
MEP+ASNIQVLLQAAEFLERREREAEHGYASLCPH SPG + RR+K P QAPGA +SGRS
Sbjct: 56 MEPLASNIQVLLQAAEFLERREREAEHGYASLCPHRSPGFIHRRICKRPPQAPGAQDSGRS 235

Query: 61 VHNELEKRRRAQLKRCLEQLRQOMPLGVDCTRYTTLSSL-RARVHIQKLEEQEQQARRLK 119
VHNELEKRRRAQLKRCLE+L+QOMPLG DC RYTTLSLL RAR+HIQKLE+QE+AR+LK
Sbjct: 236 VHNELEKRRRAQLKRCLERLKQOMPLGGDCARYTTLSSLRRARMHIQKLEDQEQRARQLK 415

Query: 120 EKLRS 124
E+LR+
Sbjct: 416 ERLRT 430

dbj|C02407|C02407 HUMGS0012279, Human Gene Signature, 3'-directed cDNA sequence.
Length = 348

Score = 97.5 bits (239), Expect = 6e-20
Identities = 51/63 (80%), Positives = 56/63 (87%)
Frame = +3

Query: 125 KQOSLOOQLEOGLPGARERERLRADSLDSSGLSSERSDSQEDLEVDVENLVFGTETE 184
KQOSLO+ QL+GL GA ERERLRADSLDSSGLSSERSDSQDE+LEVDVE+LVFG E E
Sbjct: 45 KQOSLQXWMQLRGLAGAAERERLRADSLDSSGLSSERSDSQDEELEVDES LVFGGEAE 224

Query: 185 LLQ 187
LL+
Sbjct: 225 LLR 233

Figure 17 A

BASE COUNT	130 a	234 c	258 g	106 t	5 others	
ORIGIN						
1	cagccgcttg	ctccggccgg	caccctaggg	cgcagtcggc	caggctgtcg	ccgacatgga
61	acccttggcc	agcaacatcc	aggtcctgct	gcaggcggcc	gagttcctgg	agcgccgtga
121	gagagaggcc	gagcatggtt	atgcgtccct	gtgcccgcag	cgcagtcag	gccccatcca
181	caggaggaag	aagcgacccc	cccaggctcc	tggcgcgag	gacagcgggc	ggtcagtgc
241	caatgaactg	gagaagcgca	ggaggggcca	gttgaagcgg	tgcctggagc	ggctgaagca
301	gcagatgcc	ctgggcggcg	actgtgccc	gtacaccacg	ctgagcctgc	tgcgcccgtgc
361	caggatgcac	atccagaagc	tggaggatca	ggagcagcgg	gcccgcagc	tcaaggagag
421	gctgcgcaca	aagcagcaga	gcctgcagcg	gcantggatg	cagctccggg	ggctggcagg
481	ngcgcccgag	cgggagcgnc	tgcgggcgga	cagtctggac	tcctcaggcc	tctcctctga
541	gcgctcagac	tcagaccaag	aggagctgga	ggtggatgtg	gagagcctgg	tgtttggggg
601	tgaggccgag	ctgctgcggg	gcttcgtcgc	cggccaggag	cacagctact	cgcacgtcgg
661	cggcgcctgg	ctatgatgtt	cctcaccan	ggcgggcctc	tgcctctta	ctcgttgccc
721	aagcccactt	tnc				

Figure 17B

C

>Mad3h(Putative)

MEPLASNIQVLLQAAEFLERREREAEHGYASLCPHRSPGPIHRRKKRPPQAPGAQDSGRSVHNELEKRRRAQLK
RCLERLKQQMPLGGDCARYTTLSLLRRARMHIQKLEDQEQRARQLKERLRTKQOSLQRXWMQLRGLAGAAERER
LRADSLDSSGLSSERSDSDOEELEVDVESLVFGGEAELLRGFVAGOEHSHVGGAWL

D

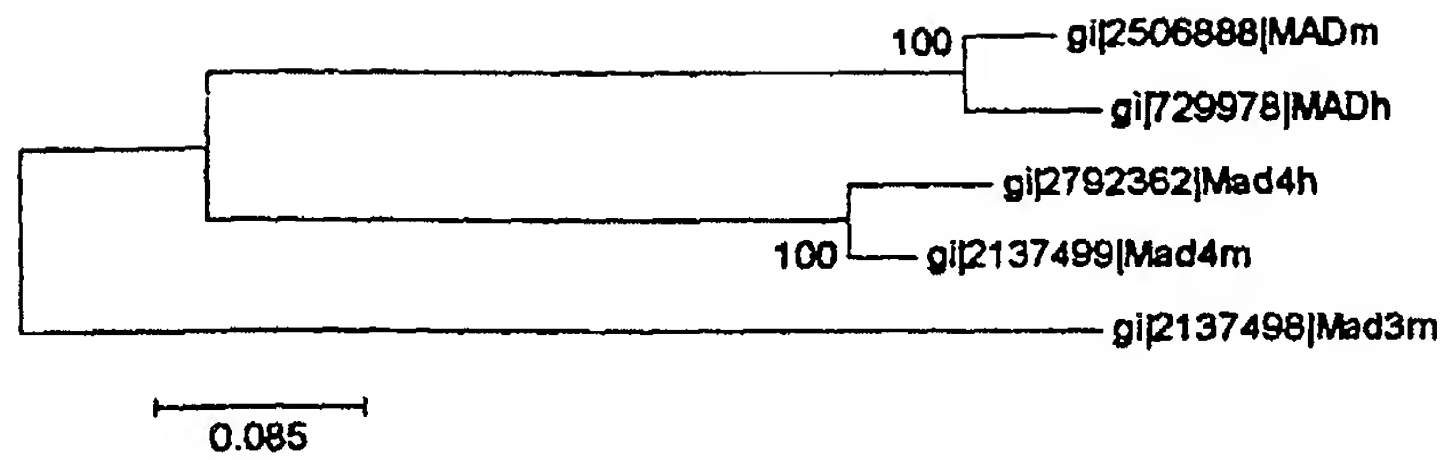
gi12506888|Mad3h|
gi1729978|Mad3h|
gi12792362|Mad4h|
gi12137499|Mad4h|
gi12137498|Mad3h|
Mad3h Putative|
MATAVGMIQVLLQAAEFLERREREAEHGYASHPYS-XGRDAFKRRNKPKONST--SSRSTHNEKWRRAHLRLCLEKLGVLPLGPSSRHHTTSL
MAAAVRMIQVLLQAAEFLERREREAEHGYASHPYNNKORDALKRRNKSKNN--SSRSTHNEKWRRAHLRLCLEKLGVLPLGPSSRHHTTSL
---MELNSLLILEAAEYLERREREAEHGYASVLPFDGDFAREKTKAAGLVKAP--MNRSSHNELEKRRRAKLRLYLEQLKQLVPLGPDSTRHTTSL
---MELNSLLILEAAEYLERREREAEHGYASHPFDGDFARQKTKTAGLVKGP--MNRSSHNELEKRRRAKLRLYLEQLKQLVPLGPDSTRHTTSL
-MEPVASNIQVLLQAAEFLERREREAEHGYASLCPHRSPGTVCRKRPPLQAPGALNSGRSVHNELEKRRRAQLKRCLEQLRQOMPLGVDCTRYTTSL
-MEPLASNIQVLLQAAEFLERREREAEHGYASLCPHRSPGPIHRRKKRPPQAPGAQDSGRSVHNELEKRRRAQLKRCLEQLRQOMPLGVDCTRYTTSL

gi12506888|Mad3h|
gi1729978|Mad3h|
gi12792362|Mad4h|
gi12137499|Mad4h|
gi12137498|Mad3h|
Mad3h Putative|
TKAKLHIKKLEDCKKAVHQIDQLQREQRHLKRLKLEKGAERT-----HDSVG-SVVSERSDSREELDVEDVDVDVDSGTDYLNQDLGWSSS-
TKAKLHIKKLEDCKKAVHQIDQLQREQRHLKRLKLEKGIERT-----HDSIG-STVSERSDSRE-----EIDVDVESTDYLTGDLWSSSS
KRAKVIKKLEEQRRALSIEQLQREHRLKRLKLEQLSVQSVR-----VRTDSTG-SAVSTD--DSEQE-----VDIEGHEFGPELDSVGS-
K-AKVIKKLEEQRRALSIEQLQREHRLKRLKLEQLSVQSVR-----VRTDSTG-SAVSTD--DSEQE-----VDIEGHEFGPELDSVGS-
R-ARVHIKKLEEQRRALSIEQLQREHRLKRLKLEQLSVQSVR-----VRTDSTG-SAVSTD--DSEQE-----VDIEGHEFGPELDSVGS-
RAARMIKKLEDQEQRARQLKERLRTKQOSLQRXWMQLRGLAGAAERERLRADSLDSSGLSSERSDSDOE-----ELEVDVESLVFG-GEAELLRGF

gi12506888|Mad3h|
gi1729978|Mad3h|
gi12792362|Mad4h|
gi12137499|Mad4h|
gi12137498|Mad3h|
Mad3h Putative|
VSDSDERGSMQSLG-SDEGYSSATVKRAKLQGGHAGLGL
VSDSDERGSMQSLG-SDEGYSSATVKRAKLQGGHAGLGL
SSDADDHYSLSGGTGGDSGFGPHCRALGRPALS-----
SSDADDHYSLSGGTGGDSGFGPHCRALGRPALS-----
SAGREHSHSTCANT-----
VAGOEHSHVGGAWL-----

Figure 17 C-D

A.



B.

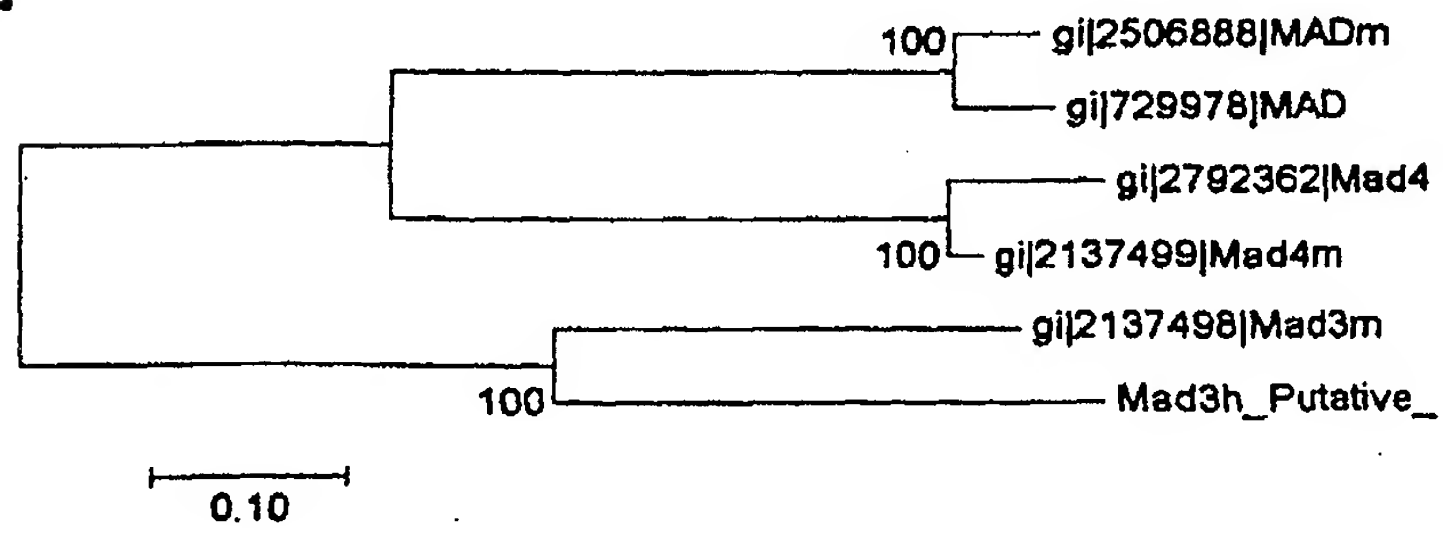


Figure 18. A-B

```

% lexsemsub.pl
% lexsemsub.pat
% revised March 17, 2000
%
% LEXICON OF SUBSTANCES AND STRUCTURES
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
:-multifile(phrase/5).
:-multifile(wdef/3).
:-unknown(_,fail).
phrase(['[',protein,['[',gamma,']'],'-','aminobutyric, acid, a], 'GA
BAA', r). % ?
phrase(['[',smallmolecule,['[',zeta,']'],1, subunit], '[zeta]1 subu
nit', r). % ?
phrase(116, protein,[116,'-',kd,fyn,'-',associated,protein], '116-k
D Fyn-associated protein',r).
phrase(116, protein,[116,'-',kd,protein], '116-kd protein',r).
phrase(3,protein,[3,'-',kinase,'-',akt], '3-kinase-Akt',r).
phrase(ability, affirmation,[ability, to], [], r).
phrase(agc,protein,[agc, protein, kinases], 'AGC', r).
phrase(akt,protein,[akt, mutant], 'Akt mutant', r).
phrase(alternative,substance,[alternative,ntf], 'alternative NTF',r
).
phrase(antibody, protein,[antibody,to,phosphotyrosine], 'anti-phosp
hotyrosine',r).
phrase(antigen, complex,[antigen,receptor], 'antigen receptor',r).
phrase(ap, protein,[ap,'-',1], 'AP-1',r).
phrase(asparagine,site,[asparagine,'-',141], 'asparagine-141',r).
phrase(b, cell,[b,cell], 'B cell', r).
phrase(b, cell,[b,cells], 'B cell', r).
phrase(b, species,[b,lymphoblastoid,cells], 'B lymphoblastoid cell
s',r).
phrase(b,cell,[b,lymphoblastoid,cells], 'B lymphoblastoid cells',r
).
phrase(b7, protein,[b7,'-',1], 'B7-1',r).
phrase(bcl,protein,[bcl,'-',2], 'Bcl-2',r).
phrase(c, protein,[c,'-',jun], 'c-Jun',r).
phrase(camk, protein,[camk, iv], 'CaMK IV',r).
phrase(casp, protein,[casp,'-',3], 'caspase-3',r).
phrase(caspase,protein,[caspase,'-',3,family,protease], 'caspase-3
family protease',r).
phrase(caspase,protein,[caspase,'-',3,precursor], 'caspase-3 precu
sor',r).
phrase(caspase,protein,[caspase,'-',3], 'caspase-3',r).
phrase(caspase,protein,[caspase,-,3], 'caspase-3',r).

```

Appendix A

```

phrase(caspase,protein,[caspase,'-',6],'caspase-6',r).
phrase(caspase,protein,[caspase,'-',7],'caspase-7',r).
phrase(catalytic,domain,[catalytic,domain],'catalytic domain',
r).
phrase(cleavage,site,[cleavage,site],'cleavage site',r).
phrase(cleavage,substance,[cleavage,products],'cleavage products',
r).
phrase(cooh,substance,[cooh,'-',terminal,fragment],'COOH-termina
l fragment',r).
phrase(crk,protein,[crk,proteins],'crk proteins',r0.
phrase(crkl,complex,[crkl,'-',c3g,complex],'crkl-c3g complex',r).
phrase(dcp,protein,[dcp,-,1],'DCP-1',r).
phrase(did,negation,[did,not],not,r).
phrase(ebv,species,['Epstein-Barr virus'],r).
phrase(epstein,species,[epstein,'-',barr,virus],'Epstein-Barr vi
rus',r).
phrase(familial,disease,[familial,alzheimer,'','',s,disease],'famil
ial Alzheimer''''s disease',r).
phrase(gene,gene,[gene,encoding,interleukin,'-',2],'gene encodin
g interleukin-2',r).
phrase(gst,protein,[gst,'-',fyn,'-',sh2],'GST-Fyn-SH2',r).
phrase(gst,protein,[gst,'-',fyn,'-',sh3],'GST-Fyn-SH3',r);
phrase(gtp,complex,[gtp,exchange,of,rap1],'GTP exchange of Rap1',
r).
phrase(guanidine,protein,[guanidine,nucleotide,'-',releasing,fac
tor,c3g],'guanidine nucleotide-releasing factor C3G',r).
phrase(guanidine,smallmolecule,[guanidine,nucleotide],'guanidine
nucleotide',r).
phrase(guanosine,smallmolecule,[guanosine,tripphosphate],'guanosin
e triphosphate',r).
phrase(guanosine,smallmolecule,[guanosine,diphosphate],'guanosine
diphosphate',r).
phrase(h4,cell,[h4,cell,line],'H4 cell line',r).
phrase(h4,cell,[h4,human,neuroglioma,cells],'H4,human,neuroglioma
,cells',r).
phrase(ha,protein,[ha,'-',,['delta,'],'',phpkb],'HA-[Delta] PHPK
B',r).
phrase(hla,protein,[hla,'-',dr7],'HLA-DR7',r).
phrase(i,protein,[i,['kappa,'],'',b,'-',,['beta,'],''], 'I[ka
ppa]B-[beta]',r).
phrase(i,protein,[i,['kappa,'],'',b,'-',,['alpha,'],''], 'I[kap
pa]B-[alpha]',r).
phrase(i,protein,[i,['kappa,'],'',b], 'I[kappa]B',r).

```

```

phrase(ice,protein,[ice,'/',ced,'-',3],'ICE/Ced-3',r).
phrase(il, gene, [il,'-',2,gene], 'gene encoding interleukin-2', r
).
phrase(il, protein, [il,'-',2], 'interleukin-2',r).
phrase(in, interm, [in, the, case, of],[], r).
phrase(in,state,[in,the,anergic,state], inactive,r).
phrase(inducible, cell, [inducible,h4,cell], 'inducible H4 cell',r
).
phrase(interleukin, protein, [interleukin,'-',2],r).
phrase(interleukin, protein,[interleukin, '-', 3], 'interleukin-3
',r).
phrase(interleukin,protein,[interleukin,'-',1,beta,converting,enzy
me], 'interleukin-1 beta converting enzyme',r).
phrase(jurkat, cell, [jurkat, cell], 'Jurkat cell', r).
phrase(jurkat, cell, [jurkat, cells], 'Jurkat cell', r).
phrase(kif3a,protein,[kif3a,'/',3,b],'KIF3A/3B',r).
phrase(lbl, cell, [lbl,'-',drf, cells], 'LBL-DR7 cells',r).
phrase(lbl,cell,[lbl,'-',dr7,cells],'LBL-DR7 cells',r).
phrase(let, protein, [let,'-',23], 'Let-23', r).
phrase(may, probability,[may, be], possible, r).
phrase(myc, protein, [myc, '-', p70s6kd3e], 'Myc-p70s6kD3E',r).
phrase(myc, protein, [myc, '-', pdk1], 'Myc-PDK1',r).
phrase(myc,protein,[myc,'-',p70s6k],'Myc-p70s6k',r).
phrase(myc,protein,[myc,'-',p70s6ke389d3e], 'Myc-p70s6kE389D3E',r)
.
phrase(myf, protein,[myf,'-',akt], 'Myf-Akt',r).
phrase(n,protein, [n,'-',methyl,'-',d,'-',aspartate, receptor], 'N
MDAR', r).
phrase(n,protein, [n,'-',methyl,'-',d,'-',aspartate], 'NMDA').
phrase(native, cell, [native,h4,cell],'native H4 cell',r).
phrase(nf, protein, [nf,'-',['kappa,'],'b], 'NF-[kappa]B',r).
phrase(nh2, site, [nh2,'-',terminal], 'NH2-terminal',r).
phrase(nh2,substance,[nh2,'-',terminal,fragment], 'NH2-terminal fr
agment',r).
phrase(nih, cell,[nih,'-',3,t3,fibroblasts], 'NIH-3T3 fibroblasts'
, r).
phrase(nih,cell,[nih,'-',3t3, fibroblasts],'NIH-3T3 fibroblasts'
,r).
phrase(normal,substance,[normal,ntf],'normal NTF',r).
phrase(nuclear, protein, [nuclear, factor, kappa, b], 'NF-[kappa]B'
, r).
phrase(p150Glued,protein,[p150Glued,-,arp1],'p150Glued-Arp1',r).
phrase(phosphate,phosphorylate2, [phosphate, incorporated, intol],

```

phosphorylate,r).

phrase(phosphatidylinositol, smallmolecule, [phosphatidylinositol,1, ' ',4, ' ',5, '- ', triphosphate], 'phosphatidylinositol 1,4,5-triphosphate',r).

phrase(phosphoinositide, protein, [phosphoinositide, '- ', dependent, protein, kinase], 'PDK1',r).

phrase(phospholipase, protein, [phospholipase,c, '- ',1], 'phospholipase C-1', r).

phrase(poly,protein, [poly, '(', adp, '- ', ribose, ')', polymerase], 'poly (ADP-ribose) polymerase',r).

phrase(polyvinylidene, structure, [polyvinylidene, difluoride, membranes], 'polyvinylidene difluoride membranes',r).

phrase(presenilin, protein, [presenilin,1], 'presenilin 1',r).

phrase(presenilin,protein, [presenilin,2], 'presenilin,2',r).

phrase(productively, state, [productively,stimulated], active,r).

phrase(protein, protein, [protein,tyrosine,kinase], 'protein tyrosine kinase', r).

phrase(protein,protein, [protein,kinase,c], 'protein kinase C',r).

phrase(ps2, substance, [ps2, '- ',ctf], 'presenilin 2 COOH-terminal fragment',r).

phrase(ps2, substance, [ps2,cleavage,fragment], 'presenilin 2 cleavage fragment', r).

phrase(pvdf, structure, [pvdf, membranes], 'polyvinylidene difluoride membranes',r).

phrase(raf, protein, [raf, '- ',1], 'Raf-1', r).

phrase(raf,protein, [raf, '- ',1], 'Raf-1',r).

phrase(rap1, complex, [rap1, '- ',gtp], 'Rap1-GTP',r).

phrase(requirement, need2, [requirement, for], need,r).

phrase(ser, smallmolecule, [ser, 19], 'Ser 19',r).

phrase(ser, smallmolecule, [ser, 23], 'Ser 23',r).

phrase(serine, substance, [serine, residues], 'serine residues', r).

phrase(src, domain, [src, homology, 2], 'Src homology 2',r).

phrase(src, domain, [src, homology, 3], 'Src homology 3',r).

phrase(srebp,protein, [srebp, '- ',1], 'sterol-regulatory element binding protein 1',r).

phrase(srebp,protein, [srebp, '- ',2], 'sterol-regulatory element binding protein 2',r).

phrase(sterol,protein, [sterol, '- ',regulatory,element, binding,protein,1], 'sterol-regulatory element binding protein 1',r).

phrase(sterol,protein, [sterol, '- ',regulatory,element, binding,protein,2], 'sterol-regulatory element binding protein 2',r).

```

phrase(t, cell, [t, '-', dr7], 't-DR7', r).
phrase(t, cell, [t, '-', drt, '/', b7, '-', 1], 't-DR7/B7-1', r).
phrase(t, cell, [t, cell], 'T cell', r).
phrase(t, cell, [t, cells], 'T cell', r).
phrase(t, complex, [t, '-', cell, receptor], 'T-cell receptor', r).
phrase(t, cell, [t, '-', dr7, cells], 't-DR7 cells', r).
phrase(t, cell, [t, '-', dr7, '/', b7, '-', 1], 't-DR7/B7-1', r).
phrase(t, complex, [t, '-', cell, antigen, receptor], 'T-cell antigen receptor', r).
phrase(threonine, aminoacid, [threonine, 229], 'threonine 229', r)

phrase(transcription, protein, [transcription, factor], 'transcription factor', r).
phrase(trypan, smallmolecule, 'trypan blue', r).
phrase(wt, protein, [wt, akt], 'WT Akt', r).
phrase(zap, protein, [zap, '-', 70], 'ZAP-70', r).
phrase(zdevd, smallmolecule, [zdevd, '-', fmk], 'zDEVd-fmk', r).
phrase(il, protein, [il, '-', 3], 'interleukin-3', r).
wdef(ab, complex, antibody).
wdef(actin, protein, actin).
wdef(activated, state, active).
wdef(active, state, active).
wdef(ad, disease, 'Alzheimer''''s disease').
wdef(agc, protein, 'AGC').
wdef(akt, protein, 'AKT').
wdef(anergic, state, inactive).
wdef(anergic, state, inactive).
wdef(anergy, state, inactive).
wdef(antibody, complex, antibody).
wdef(antigen, substance, antigen).
wdef(aop, protein, 'Aop').
wdef(apoptosis, process, apoptosis).
wdef(bad, protein, 'BAD').
wdef(c3g, protein, 'C3G').
wdef('ca2+', smallmolecule, 'Ca2+').
wdef(cas, protein, 'Cas').
wdef(caspase, protein, caspase).
wdef(caspase, protein, caspase).
wdef(cbl, protein, 'Cb1').
wdef(ccrsrh, protein, 'CCRSrh').
wdef(cd28, protein, 'CD28').
wdef(cells, structure, cell).
wdef(cholesterol, smallmolecule, cholesterol).

```



```
wdef(cpp32,protein,'CPP32').
wdef(crkl, protein, 'CrkL').
wdef(ctf,substance,'COOH-terminal fragment').
wdef(cytokine, smallmolecule, cytokine).
wdef(cytosol, structure, cytosol).
wdef(djnk,protein, 'DJNK').
wdef(djun, protein, 'DJun').
wdef(dynamitin,protein,dynamitin).
wdef(erk, protein, 'ERK').
wdef(eto,smallmolecule,'ETO').
wdef(etoposide,smallmolecule,etoposide).
wdef(fad,disease,'familial Alzheimer''''s disease').
wdef(fyn, protein, 'Fyn').
wdef(gdp, smallmolecule,'GDP').
wdef(gelsolin,protein,gelsolin).
wdef(gp120,protein,'gp120').
wdef(grb2, protein, 'Grb2').
wdef(gst, protein, 'glutathione S-transferase').
wdef(gtp, smallmolecule,'GTP').
wdef(hsp70,protein,'HSP70').
wdef(human, species, human).
wdef(ikk, protein, 'IKK').
wdef(inactivated, state, inactive).
wdef(inactive,state, inactive).
wdef(jnk, protein, 'JNK').
wdef(jnk, protein, 'JNK').
wdef(jnk2, protein,' JNK2').
wdef(kap3,protein,kap3).
wdef(kdakt, protein, 'KDAkt').
wdef(kinase,protein, kinase).
wdef(kinectin,protein,kinectin).
wdef(klc,protein,klc).
wdef(lamin,protein,lamin).
wdef(myosins,protein,myosins).
wdef(nmdar,protein, 'NMDAR').
wdef(nmdar2b, protein, 'NMDAR2B').
wdef(ntf,substance,'NH2-terminal fragment').
wdef(p70s6k, protein, p70s6k).
wdef(p78s6k, protein, p78s6k).
wdef(parp,protein, 'poly(ADP-ribose)polymerase').
wdef(pdk1, protein, 'PDK1').
wdef(peptides, protein, peptide).
wdef(pkb, protein, 'PKB').
```

	206	979	-178	-352	-36	372	585	-635	438	-130	677	-164	41	-73	335	54	27	-12	-255	97
13	-76	-10390	-4298	-732	-1329	2508	-279	*	*	*	2975	440	751	-478	271	649	-518	125	545	2395
	1891	484	159	350	1092	-1	939	-607	452	-798										
	206	979	-178	-352	36	372	585	-635	438	-130	677	-164	41	-73	-335	-54	27	-12	-255	97
-	-53	-10402	-4831	-732	1329	-2638	-253	*	*	*										
14	-1544	117	99	-433	1201	-927	779	-558	-17	-318	-25	-1196	812	225	-301	-421	440	735	-2569	653
-	206	979	-178	-352	-36	372	585	-635	438	-130	677	-164	41	-73	-335	-54	27	-12	-255	-97
-	20	-10421	-6282	-732	-1329	-2245	-342	*	*	*										
15	-271	-1402	122	84	621	-135	786	-1396	-125	16	-835	-1064	657	-830	-798	-173	82	811	558	618
-	206	979	-178	-352	-36	372	585	-635	438	-130	677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-23	-10502	-6072	-732	-1329	-3329	-151	*	*	*										
16	-1475	-1395	305	1025	1081	360	-400	-870	-768	-809	-3051	695	613	-548	-114	-1142	151	-98	1927	-111
-	206	979	-178	-352	-36	372	585	-635	438	-130	677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-41	-10494	-5199	-732	-1329	-3725	-113	*	*	*										
17	-945	24	278	129	1415	-574	164	-1466	-164	515	-238	833	463	-210	-2677	-785	-979	905	-25	-2438
-	206	979	-178	-352	-36	372	585	-635	438	-130	677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-118	-10455	-3667	-732	-1329	-3067	-183	*	*	*										
18	-903	83	828	842	1676	-1211	-1689	519	-65	-698	-2951	-483	349	886	-841	-1224	-1664	193	590	-247
-	206	979	-178	-352	-36	372	585	-635	438	-130	677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-58	-10373	-4702	-732	-1329	-3019	-190	*	*	*										
19	-604	-182	-2092	-158	1851	-1895	-84	840	856	-219	-2944	-188	607	-143	-763	-473	290	-2187	1413	114
-	206	979	-178	-352	-36	372	585	-635	438	-130	677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-2	-10365	-11365	-732	-1329	-2675	-246	*	*	*										
20	-946	873	129	-185	1399	-1954	-294	255	250	513	-1340	-2446	100	-1248	1200	-2351	775	-926	635	-188
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-	-2	-10435	-11435	-732	-1329	-2639	-252	*	*	*										
21	-985	-1396	77	-695	1037	-2004	-205	-216	636	647	-3052	1080	541	-171	-168	-2430	51	-405	-2630	1250
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22	-2205	-1431	391	417	1650	-2038	1141	-697	-144	490	1149	-706	284	-2483	-2077	-1155	-661	295	282	1418
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-	-52	-10537	-4839	-732	-1329	-3319	-152	*	*	*										
23	190	-1396	119	-627	1701	-2003	-73	-2084	265	55	-112	-956	648	617	937	-2429	-320	-172	-2630	746
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-	-2	-10494	-11494	-732	-1329	-2740	-234	*	*	*										
24	-1493	461	222	960	1719	-1229	496	13	-767	524	-1910	-2576	-387	-194	758	-1633	-991	233	-2667	246
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26	-472	134	-420	-549	1604	-2022	348	-454	826	46	-155	711	-224	874	16	-2448	-1125	-215	-2649	1130
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-	-38	-10517	-5292	-732	-1329	-2966	-198	*	*	*										
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-	-75	-10508	-4318	-732	-1329	-2826	-219	*	*	*										
28	-2151	-1378	-417	288	1496	-1985	-15	-869	-693	524	-1250	699	483	408	440	-1438	-2330	-465	-2612	2022
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	-56	10512	4750	732	-1329	-2887	-210	*	*	*	*	*	*	*	*	*	*	*	*	*
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33	-934	478	634	-224	-756	-692	-1785	-479	-219	-175	443	725	1139	780	829	-1023	750	-851	-2625	-2467
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35	-2141	-1368	296	-86	1186	-30	-344	-919	-611	-13	-1005	-1858	478	760	406	-394	-21	-139	-2602	1782
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39	-873	2186	816	899	-809	-560	-353	-194	-967	-222	137	-2520	-539	1020	-423	280	-833	447	-2610	1012
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66	869	73	53	-218	-883	-312	235	-385	-827	211	1454	-947	265	395	-1852	448	-1307	-1321	-2689	1346
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-1	-10565	-11565	-732	-1329	-3499	-134	*	*											
67	530	-1409	906	696	346	-831	-1849	-132	333	810	235	-1312	-610	-128	-2069	-212	-458	-476	-2689	1162
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-50	-10565	-4899	-732	-1329	-3499	-134	*	*											
68	335	-37	-2572	239	-823	-415	-1808	-811	-97	1312	361	-819	518	684	-533	-97	-2367	174	-2648	857
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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69	629	-1455	-581	-370	261	622	328	-1326	-1996	749	-321	-356	172	-252	-192	174	-471	411	-2689	-1079
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-1	-10565	-11565	-732	-1329	-3499	-134	*	*											
70	1036	647	514	-121	-314	483	-1849	-375	12	32	-3111	-2599	79	-1	-1033	262	-1491	-904	-2689	1300
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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	206	979	178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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72	182	179	862	536	-58	187	592	310	609	824	-3111	-2599	-817	-1270	-1209	-1332	-1464	-201	-2689	450
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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73	192	-816	663	827	-803	-25	-1849	-1015	-59	767	-2917	-1344	-1350	1458	-1952	-1280	-1433	681	-2689	1025
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	-1	-10565	-11565	-732	-1329	-3499	-134	*	*											
74	113	-752	832	-1098	-1045	-684	-101	-870	-1003	1356	-428	-356	-57	905	-1262	-358	-1464	-57	-2689	952
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	-1	-10565	-11565	-732	-1329	-3499	-134	*	*											
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	-45	-10565	-5063	-732	-1329	-3499	-134	*	*											
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	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-76	-10521	-4296	-732	-1329	-2666	-247	*	*											
77	-2167	-806	991	605	639	186	964	-3009	249	166	-1593	-701	-1510	1126	-696	-549	-41	-864	-2628	1470
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-66	-10492	4511	-732	-1329	-1690	-116	*	*											
78	-1127	-1340	437	-2672	278	668	454	-80	220	-118	-2996	-2484	-189	724	205	73	133	675	-1234	640
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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79	-	414	490	839	635	-336	914	266	-1919	202	-142	188	-2457	1287	-464	-2628	-2347	-71	-40	246	171
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-	-	-39	-10395	5261	732	-1329	-2683	-244	*	*											
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-	-	-55	-10425	-4757	-732	-1329	-3840	-104	*	*											
81	-	-904	-1294	925	353	-884	-322	875	188	883	262	-565	187	811	-640	-874	-1056	-2217	389	-2528	789
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-	-	-62	-10370	-4599	-732	-1329	-3942	-97	*	*											
82	-	488	1244	748	1210	-2260	-1143	862	-2859	122	-357	-2900	747	361	-1079	-804	-135	-117	-222	683	323
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83	-	1102	-1307	-1216	870	-740	701	94	515	285	-628	-433	-2451	310	1477	-831	-343	-972	-56	-2541	1048
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84	-	-2009	141	-386	1064	98	-526	1401	-1748	-78	-559	920	311	-2174	414	-608	441	658	329	636	-1264
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-	-	-49	10299	-4953	732	-1329	-3267	-158	*	*											
85	-	2004	600	289	-77	-2246	-626	1465	-53	602	377	522	-706	501	-270	-210	-681	-880	273	859	1256
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87	-	993	-1205	729	554	260	-85	-1599	-335	1342	-1161	-181	-46	-52	-443	545	367	-1510	303	168	-829
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88	-	1434	-1245	-306	43	-1452	-780	335	-1199	393	368	-12	-351	171	291	271	123	39	1060	626	28
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91	-	-2000	651	-173	697	558	-678	769	-648	-692	368	90	683	906	639	-814	-393	-699	-36	468	-954
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92	-	-288	-1401	-73	773	-816	-1086	159	-241	1958	55	-3056	-1098	-540	-380	185	-867	-916	-2392	875	989
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93	-	-885	-1433	-1831	318	-845	-1596	887	-60	926	-65	199	-661	598	858	1238	-804	-268	-1158	1739	-86
-	-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-	-105	-10539	-3850	-732	-1329	-2445	-293	*	*											
94	-	-279	56	408	990	1553	-741	-687	-1509	750	-526	598	507	-302	-1042	521	-938	-1081	-211	-2630	259
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95	-	232	1257	-690	477	1494	-1985	1307	-997	53	382	1300	-881	-1297	710	794	-2411	-1073	-990	-2612	-967
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96	277	74	10473	-11473	732	-1329	3753	-111	*	*	96	-409	274	3034	-1327	1332	1059	463	255	636	251	2087	1264
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	31	10506	-5602	-732	-1329	-3088	-181	*	*														
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99	44	10500	-5097	-732	-1329	-3684	-116	*	*														
	182	89	-656	486	120	-1537	-1760	-717	724	431	943	193	156	-416	149	-49	-1067	264	-53	-1237	-97	-97	
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100	850	486	-563	-33	-2372	1964	108	-451	118	648	-1225	-2500	-259	1173	547	-610	-365	20	-555	556	-97	-97	
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	76	10451	-4314	-732	-1329	-2299	-328	*	*														
	1362	212	829	-951	-918	-1446	161	-755	127	1027	476	-528	-954	-386	760	853	-345	-2340	10	769	-97	-97	
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102	154	10470	-3316	-732	-1329	-3579	-126	*	*														
	828	-1256	241	1342	-2271	1044	1495	-276	1462	-474	816	-2399	50	54	-881	473	-2208	-1178	620	-1330	-97	-97	
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104	948	-1207	420	902	272	-617	681	-1361	536	20	1242	-2350	-2145	458	-38	683	503	1040	2441	898	-97	-97	
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	150	-1333	375	292	-140	-1286	-1727	336	606	175	486	-2476	-390	-108	656	-1356	138	466	594	359	-97	-97	
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	202	-1412	-602	540	-559	-274	370	455	1648	-1957	960	-1014	-373	631	73	-54	-1038	-310	-405	-961	-97	-97	
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	335	54	27	-12	-255	-97	-97	-97	
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	144	-1567	-588	1058	-453	-2175	-1962	-350	1423	-283	1484	-306	-529	223	-130	-579	519	-2559	-182	-166	-97	-97	
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	873	-1589	111	1208	-345	-2196	337	-59	862	385	272	-2733	-369	1261	-100	-642	-147	-593	343	-1178	-97	-97	
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	7	-1555	-249	760	-602	-729	1103	-1438	-48	818	-1413	-543	-755	1309	774	-711	-126	-1520	-503	-524	-97	-97	
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112	1	353	-681	857	-605	-507	938	704	838	27	372	-614	-762	24	-112	-1229	219	-938	97	213	-97	-97	

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-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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DESC

LENG 75

ALPH Amino

RF no

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COM [converted from an old Plan9 HMM]

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DATE Mon Mar 8 11:42:18 1999

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-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-6	-8617	-9617	-732	-1329	-2913	-205	*	*	*	*	*	*	*	*	*	*	*	*	*
41	-234	1704	-235	-1555	-1238	-504	-617	-975	1275	-139	-1879	-30	-1162	-436	-1537	994	342	549	1284	-1299
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-6	-8617	-9617	-732	-1329	-2913	-205	*	*	*	*	*	*	*	*	*	*	*	*	*
42	-997	1665	-1381	-835	-111	1090	-617	-1838	368	-1333	893	-1367	567	-21	-1537	1041	427	317	13	-1299
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-6	-8617	-9617	-732	-1329	-2913	-205	*	*	*	*	*	*	*	*	*	*	*	*	*
43	-101	1922	-1381	-1555	423	-830	-617	-1838	-765	-351	116	-1367	14	-1275	-196	184	2009	697	-1457	-1299
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-67	-8617	-4553	-732	-1329	-2913	-205	*	*	*	*	*	*	*	*	*	*	*	*	*
44	1268	2174	-1346	-1519	-119	-795	-582	-1802	15	-946	-1844	-523	-168	999	-1502	-1221	1091	392	1193	57
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-67	-8549	-4558	-732	-1329	-3040	-187	-1768	1501	161	-1809	-634	-89	1109	-1467	205	-73	226	-1387	176
45	-502	1983	-1311	-283	-1168	-760	-547	-1768	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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-	-78	-8478	-4319	-732	-1329	-2699	-241	*	*	*	*	*	*	*	*	*	*	*	*	*
46	-264	-131	-1289	-1463	-1146	-738	-525	-1746	58	415	-1787	-1275	-475	603	-1445	1749	615	34	1973	-1207
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-	-85	-8431	-4196	-732	-1329	-2786	-226	*	*	*	*	*	*	*	*	*	*	*	*	*
47	406	-111	-1269	-990	-297	-718	-505	-1726	44	252	-1767	-1255	-586	37	-1425	16	-121	1642	1487	1045
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-	-76	-8409	-4370	-732	-1329	-3178	-169	*	*	*	*	*	*	*	*	*	*	*	*	*
48	61	1314	-1230	-1404	-415	-680	-467	-1687	732	-123	192	377	-787	-1124	-1387	674	1402	-67	1824	-1148
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-	-7	-8333	-9333	-732	-1329	-2049	-399	*	*	*	*	*	*	*	*	*	*	*	*	*
49	-963	3110	-1348	-1521	-1205	-797	-584	-1805	954	-642	-1846	-614	438	-398	-1504	598	832	-205	1484	744
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50	-97	1704	-74	-1489	-1173	-349	-552	-1772	87	173	-1813	126	-119	-519	-1472	267	1686	-315	540	253
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-	-62	-8485	-4682	-732	-1329	-3064	-184	*	*	*	*	*	*	*	*	*	*	*	*	*
51	-463	1118	-464	-1458	912	-733	-520	-1741	20	249	-325	-1270	1128	-1178	-1440	266	297	-297	-1360	1994
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-	-81	-8423	-4267	-732	-1329	-3169	-170	*	*	*	*	*	*	*	*	*	*	*	*	*
52	362	2088	-858	-711	-380	-481	-481	-1701	-158	-537	-1743	547	212	64	-1401	1252	-157	174	-1321	212
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-71	-8344	-4484	-732	-1329	-3408	-143	*	*	*	*	*	*	*	*	*	*	*	*	*
53	-826	1153	-1210	-963	98	-659	-446	-1371	1021	264	-1708	-1196	1460	1591	-1366	-579	469	-259	-1286	-1128
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-69	-8270	-4528	-732	-1329	-3485	-135	*	*	*	*	*	*	*	*	*	*	*	*	*

54	-315	1857	-385	-923	-1038	-630	-417	-1637	-564	1160	827	550	323	679	-1337	25	-339	-834	1278	-1099
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-7	-8205	-9205	-732	-1329	-3696	-116	*	*	*	*	*	*	*	*	*	*	*	*	*
55	444	754	-439	-1354	908	-630	-417	-1057	539	1518	-1679	-519	-269	129	-1337	-1056	-976	-185	-1257	-1099
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56	-203	2112	-1181	-1354	-1038	-630	-417	-1637	1186	-182	1182	1636	-405	-1075	-1337	-1056	-81	504	1184	-1099
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-	-7	-8205	-9205	-732	-1329	-3696	-116	*	*	*	*	*	*	*	*	*	*	*	*	*
57	-143	-23	-1181	-1354	695	-630	-417	-1637	1796	-421	-1679	-1166	-962	1183	-1337	533	623	47	-1257	-1099
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58	-796	2846	-187	-1354	-382	-630	-417	-1637	427	1166	494	-1166	-962	-188	-1337	137	412	-834	-1257	-61
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-	-211	-8205	-2913	-732	-1329	-3696	-116	*	*	*	*	*	*	*	*	*	*	*	*	*
59	482	1662	-1072	-1246	1741	-521	-308	-1529	-456	-328	-1570	-1058	926	879	-1228	-184	18	-344	867	78
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-	-9	-7972	-8972	-732	-1329	-3825	-106	*	*	*	*	*	*	*	*	*	*	*	*	*
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-	-88	-7972	-4185	-732	-1329	-3825	-106	*	*	*	*	*	*	*	*	*	*	*	*	*
61	461	1019	-1033	-1207	-891	-483	-270	-919	-417	-636	88	-1019	171	2454	-929	-909	933	-55	-1110	-951
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-	-9	-7883	-8883	-732	-1329	-3876	-102	*	*	*	*	*	*	*	*	*	*	*	*	*
62	46	2054	-1033	-1207	-891	-483	-270	-448	755	1400	-1531	-1019	-814	592	-1190	-52	-528	-502	-1110	-951
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-	-9	-7883	-8883	-732	-1329	-3876	-102	*	*	*	*	*	*	*	*	*	*	*	*	*
63	1236	125	-1033	-1207	-891	-50	-270	-311	-49	-617	-1531	-1019	828	-355	-1190	-480	1097	-697	2591	-951
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-	-106	-7883	-3915	-732	-1329	-3876	-102	*	*	*	*	*	*	*	*	*	*	*	*	*
64	-195	2183	-989	-1163	-846	-438	-225	-998	1707	-657	-1487	-975	-770	-883	-1145	-864	160	1473	681	-907
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-	-10	-7775	-8775	-732	-1329	-3960	-96	*	*	*	*	*	*	*	*	*	*	*	*	*
65	-605	1556	-989	-1163	-846	-235	-225	-1446	66	-488	-1487	746	893	901	-1145	-273	1536	-94	404	-907
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66	-101	3140	-363	-1149	-833	-425	-212	-1432	-359	143	-1473	-961	292	-870	-1132	508	-195	1020	-1052	-894
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-	-69	-7738	-4564	-732	-1329	-3996	-93	*	*	*	*	*	*	*	*	*	*	*	*	*
67	-565	1100	-949	-1123	-807	-399	-186	-1406	-333	-690	-1447	-935	1798	-844	-838	-239	936	95	2283	1279
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-	-280	-7670	-2545	-732	-1329	-4034	-91	*	*	*	*	*	*	*	*	*	*	*	*	*
68	-440	333	-825	-998	-682	-274	-61	-778	-208	514	-1323	-810	24	1	-199	-372	-129	1847	-901	-743
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-	-103	-7341	-3997	-732	-1329	-4148	-84	*	-178	-182	-1292	-780	-575	1998	903	-178	-360	-628	-870	-712
69	-410	364	448	-564	159	-243	-30	-431	-178	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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-	-210	-7154	-2960	-732	-1329	-4319	-74	*	*	-503	-1197	-684	-480	-593	-855	942	-494	1818	-775	-617
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-	-402	-6982	-2089	-732	-1329	-4478	-66	*	*	-516	-1063	-36	-345	-459	-444	879	-160	146	-641	-483
73	-180	593	1278	-305	-422	-14	199	-1021	52	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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-	-212	-6474	-2998	-732	-1329	-4535	-64	*	*	-466	-1012	-500	-295	-408	-670	1646	-97	-348	-590	-432
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-	-170	-6305	-3348	-732	-1329	-4604	-61	*	*	-412	-958	-446	-241	-355	-617	-336	1973	-294	-537	-378
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-	*	*	*	*	*	*	*	*	0	*	*	*	*	*	*	*	*	*	*	*

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13	-1238	-2001	418	1334	-3016	474	1189	-3615	211	-1220	-3657	-1180	2353	340	-1379	-1466	-1381	-1271	1291	-795
-	206	979	178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	54	27	12	-255	-97
-	-32	-11195	-5544	732	-1329	-3719	-114	*	*	*	*	*	*	*	*	*	*	*	*	*
14	-1935	-1972	-247	2067	-506	-198	2302	-714	-566	-1182	-3628	574	-65	533	-27	26	-2925	-2371	1179	-3048
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15	-1532	-1989	-855	51	-584	-1179	3397	-723	-653	-1299	-3645	172	1157	311	-1351	-800	-1861	-2981	3783	-3065
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16	-1322	1176	-1153	3326	-3010	-1807	2521	-1543	207	-786	-3651	-1171	-141	-1020	-1354	497	-1358	-1255	4727	-1014
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17	-945	1463	-1405	486	-3050	383	3156	-3649	1451	-1692	-3690	-956	756	-565	-2490	-1661	-846	-1099	2092	7
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18	-2796	947	276	-939	-801	-123	-102	42	2007	268	-3679	-238	-4	50	-1201	-1413	-379	143	-3257	448
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19	-258	161	2345	-3321	1273	34	-396	-748	36	-1982	-3645	-1511	760	-756	-1094	-1171	-405	-562	-3223	1078
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22	1268	1738	-75	2663	-3097	-53	-2476	1833	-696	-1075	-3738	-1415	-1331	843	-692	-377	278	246	3316	904
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	54	27	12	255	97
-	-23	-11287	-6029	-732	-1329	-3033	-188	*	*	*	*	*	*	*	*	*	*	*	*	*
23	1809	1839	-794	2654	-3082	59	-325	-3682	1043	-1951	-595	1343	-812	1094	-3381	217	-986	-3059	-3301	-875
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-1	-11270	12270	-732	-1329	-2525	-275	*	*	*	*	*	*	*	*	*	*	*	*	*
24	-1643	1678	-1454	-2187	-3099	1756	-2478	-1657	1918	-900	-3740	783	-58	347	-1282	-189	479	-3075	-3318	-3160
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-23	-11288	-6001	-732	-1329	-1411	-681	*	*	*	*	*	*	*	*	*	*	*	*	*
25	-140	-2110	-561	542	-3125	2055	-1531	-834	75	-2055	-2090	418	687	806	-1293	-211	-318	-1601	-3344	-877
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-1	-11316	12316	-732	-1329	-1896	-451	*	*	*	*	*	*	*	*	*	*	*	*	*
26	-1465	-2137	535	1501	-3152	-78	-1552	-353	-1080	-1199	-1353	859	257	1359	1466	-233	-555	-1636	-3371	-3213
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-	-1	-11346	-12346	-732	-1329	-1977	-423	*	*	*	*	*	*	*	*	*	*	*	*	*
27	-2931	-2157	621	-2753	-3173	-2765	752	906	258	-816	-3813	83	544	2194	2245	-465	-2466	-1666	-3391	-408
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-22	-11370	-6065	-732	-1329	-2450	-292	*	*	*	*	*	*	*	*	*	*	*	*	*
28	-576	-2137	75	1927	-365	-2744	18	329	-2678	-1998	-3792	-513	-175	2953	-698	1614	-1502	-809	-3371	-3213
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-1	-11346	-12346	-732	-1329	-1977	-423	*	*	*	*	*	*	*	*	*	*	*	*	*
29	-2931	-2157	-238	-980	-3173	-2765	-396	237	-284	-1475	-3813	-1347	2286	702	-1530	2054	-312	-950	-3391	-3233
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-1	-11370	-12370	-732	-1329	-2450	-292	*	*	*	*	*	*	*	*	*	*	*	*	*
30	-608	-2157	64	-980	-3173	-1556	306	1281	574	-3267	-3813	-1670	2658	-3210	-1530	187	-1532	759	-3391	-3233

25

46	-29	-11141	-5674	732	-1329	-2410	301	*	63	-503	150	-3622	-437	1099	746	148	1303	131	1032	3200	199
	538	1966	-307	-3297	-316	-1294	540	*	-635	438	-130	-677	-164	41	-73	-335	54	27	-12	-255	-97
	206	979	-178	-352	-36	372	585	*													
	-63	-11149	-4559	-732	-1329	-1451	-651	*													
49	-1553	-2040	-1352	-660	104	-588	1542	256	-1044	-1036	-1036	-1296	520	-1213	429	-2529	1328	-1138	1735	977	-3116
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
	-71	-11236	-4401	-732	-1329	-2237	-344	*													
50	-738	-59	-1334	-1316	-3024	-835	-210	-1534	-2550	-80	-166	-901	-901	-1195	225	-3323	1881	-209	118	-3243	2673
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
	-307	-11202	-2384	-732	-1329	-1407	-683	*													
51	-32	-811	-273	-1496	-2856	999	-153	-670	-2382	-1322	-431	1884	-1884	-1531	-951	-2265	-830	-2793	-1817	-3075	3232
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
	-422	-11016	-1983	-732	-1329	-3349	-149	*													
52	-1182	-1478	-76	315	-79	438	71	-2066	-889	9	-3134	1354	1258	-723	-2792	126	-337	-1799	1250	1585	
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
	-160	-10589	-3258	-732	-1329	-2636	-253	*													
53	-31	-1510	1294	-569	511	665	956	-908	352	-140	-3166	1677	-2449	-2562	-1074	74	-1263	-879	488	-2586	
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
	-13	-10628	6893	732	-1329	-2191	-357	*													
54	19	-1734	1491	-1100	-890	-429	1619	-3348	646	-862	-956	845	1027	-74	-437	-118	-151	-1061	-821	-606	
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
	-28	-10893	-5758	-732	-1329	-915	-1090	*													
55	821	-2040	1754	-1269	-1073	-77	15	-706	-704	-949	140	847	103	504	-904	-366	434	-2025	-3274	99	
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	12	-255	97
	-14	-11239	-6774	-732	-1329	-1143	-870	*													
56	170	555	-3279	108	-357	147	-2515	-698	-98	-669	-2088	-1789	-77	2254	-987	1092	207	319	3355	-3197	
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	12	355	97
	-23	-11329	6019	-732	-1329	-1793	-491	*													
57	1635	430	2528	-808	1006	-1430	-2535	4	675	-1517	226	732	-443	-32	-3193	215	220	1998	109	-505	-2142
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
	-29	-11351	5699	-732	-1329	-1843	-471	*													
58	-542	15	-1604	11	315	-344	-2535	-61	-113	-1794	216	532	-32	-3193	215	-503	1516	428	-1555	-3243	-941
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
	-148	-11351	3360	-732	-1329	-2735	-235	*													
59	-1645	-995	519	-558	-351	-802	-293	-806	410	471	540	1332	-763	-1092	-503	-335	-54	27	-12	-255	-97
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
	-45	-11206	-5039	732	-1329	-1356	-715	*													
60	-818	819	1444	269	532	-284	-325	-1360	-444	1413	-3727	-51	-1437	-317	-191	-831	876	357	-426	-3147	
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
	-27	-11274	-5791	-732	-1329	-1526	-615	*													
61	-2872	59	-378	-514	-334	-852	1011	1859	-2144	-1042	-1300	643	-3037	-1140	1746	-1717	781	186	982	-2101	
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
	-65	-11304	4508	-732	-1329	-1487	-636	*													
62	-1775	87	556	-1407	-313	-456	517	2077	-2138	-137	-152	1444	-3026	-24	-1448	-1893	-636	1110	726	-862	
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
	-1	-11291	12291	-732	-1329	-2683	-244	*													
63	-2866	-2093	1437	-2214	-316	-828	579	-107	306	1116	-160	2516	-3031	-2257	-23	-415	-59	-812	-1291	-578	
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
	-86	-11297	4116	-732	-1329	-2052	-398	*													
64	-860	-2022	1321	-3353	-1003	-830	641	-3637	-405	-373	-3678	3282	-2961	-180	-1333	-3055	363	666	-3256	-743	
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
	-26	-11215	5617	-732	-1329	-2531	-274	*													

65	2795	-42	1598	3353	-3037	1640	1069	-1520	-1225	-2341	454	2722	90	-3074	1333	1370	1101	92	3256	3098
	206	979	178	352	-36	372	585	-635	438	-130	677	-164	41	-73	-335	54	27	12	-255	97
	-52	-11215	-4826	-732	-1329	-3122	-176	*	*	*	*	*	*	*	*	*	*	*	*	*
66	-1450	-1968	-3126	-427	792	2220	2779	-516	-44	-3078	3624	-255	1103	298	-418	-1615	-459	-667	-3202	3044
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-28	-11152	-5713	-732	1329	-1493	-633	*	*	*	*	*	*	*	*	*	*	*	*	*
67	-38	-2062	-444	3393	644	-142	3521	-1577	-854	-646	3718	-246	-1561	-381	-2026	1115	-928	205	-3296	-750
	206	979	-178	352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-1	11261	12261	-732	-1329	-2368	-311	*	*	*	*	*	*	*	*	*	*	*	*	*
68	1258	445	487	-1643	2102	-669	847	-2799	-517	-2388	-2077	-1242	-2318	273	-3400	-62	1060	522	-3320	-3161
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-24	-11288	-5934	-732	-1329	-2274	-334	*	*	*	*	*	*	*	*	*	*	*	*	*
69	-952	-1117	1413	-371	2574	-1314	1041	704	-1311	-856	-174	775	-506	-548	83	-967	-507	157	315	-838
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-24	-11288	-5934	-732	-1329	-1854	-467	*	*	*	*	*	*	*	*	*	*	*	*	*
70	-1435	-2108	233	-569	-1130	-837	324	-125	-669	-1749	1011	2132	-1307	1173	-2582	133	-1464	1591	-1312	-3184
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-47	-11314	-4986	-732	-1329	-1898	-451	*	*	*	*	*	*	*	*	*	*	*	*	*
71	-1361	107	348	607	-1336	415	-292	-433	-1101	-519	-840	694	-3029	-170	-1428	-828	-993	2009	313	8
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-72	-11294	-4363	-732	-1329	-2786	-226	*	*	*	*	*	*	*	*	*	*	*	*	*
72	-2790	-1074	11	1631	2312	1164	-2411	-204	-2558	-212	-2044	-680	-536	-523	-858	-1364	-71	-2446	-3251	-1478
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-53	-11208	-4802	-732	-1329	-2476	-286	*	*	*	*	*	*	*	*	*	*	*	*	*
73	-1473	1990	1066	128	2432	25	-2384	-2736	453	-75	-3646	-719	343	-940	-1988	23	-535	-2425	980	318
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-55	-11177	4749	-732	-1329	-2145	-370	*	*	*	*	*	*	*	*	*	*	*	*	*
74	-803	-1990	2823	-1091	-792	334	-2384	-3604	-999	372	-392	-136	-725	-3042	-1988	-565	691	-2981	-3224	-684
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-77	-11177	4285	-732	-1329	-1824	-479	*	*	*	*	*	*	*	*	*	*	*	*	*
75	-575	-1997	2291	-2167	-2188	83	-1457	-3611	-264	-673	-3652	810	639	-3049	-1529	1227	-184	-1435	-3231	429
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-172	-11185	3159	-732	-1329	-2139	-372	*	*	*	*	*	*	*	*	*	*	*	*	*
76	-700	-1904	1671	2010	-676	-735	847	-1473	-570	-470	-3560	-295	-370	660	-1284	1836	-1020	-551	-3138	143
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-309	-11086	2378	-732	-1329	-2875	-211	*	*	*	*	*	*	*	*	*	*	*	*	*
77	-238	-639	1365	-1363	-2698	30	-1036	-1343	84	-455	-549	330	-284	2715	-1440	111	-862	-2674	-2917	-2759
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-220	-10835	-2828	-732	-1329	-2628	-255	*	*	*	*	*	*	*	*	*	*	*	*	*
78	-1227	-1596	2359	-735	-427	320	-1990	-1265	878	-542	1142	399	-914	-2648	613	-2030	-2548	-2587	-2830	1132
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-1	-10733	-11733	-732	-1329	-1664	-547	*	*	*	*	*	*	*	*	*	*	*	*	*
79	480	-1846	-484	-2419	-2861	133	811	-2513	1916	-2956	-1769	-292	-187	232	-50	916	-2134	-691	-3080	1621
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-74	-11022	-4334	-732	-1329	-1111	-897	*	*	*	*	*	*	*	*	*	*	*	*	*
80	1593	-1989	3147	-2590	-218	-250	-2383	-1114	-1234	-399	1046	-472	-138	-207	-552	-139	-900	1374	-3223	1106
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-8	-11182	-7685	-732	-1329	-918	-1087	*	*	*	*	*	*	*	*	*	*	*	*	*
81	-697	-1141	-3282	-1706	-47	-104	-355	812	-738	1213	-2094	-805	-459	-731	-464	-628	-814	1514	575	85
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-46	-11333	5026	-732	-1329	-2755	-231	*	*	*	*	*	*	*	*	*	*	*	*	*
82	-2058	-2080	-629	2	-88	-859	546	321	1106	1355	627	-3224	-1489	526	-423	-625	153	-162	-3314	-2105

83	206	979	-178	352	-36	372	585	-635	438	-130	677	-164	41	-73	335	54	27	-12	-255	-97
	22	-11283	-5097	732	-1329	-2550	-270	*	*											
	372	-2055	734	973	-585	1665	-2459	-509	1592	-51	-520	-1212	-475	-798	-273	378	-130	-1269	3299	-3141
	206	979	178	352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	255	-97
	-1	-11265	-12265	732	-1329	-2088	-387	*	*											
84	960	-2093	-181	-2705	-3108	2776	1648	-759	-2635	-821	-3749	-1250	-193	-1099	-1245	122	-550	-1772	-3327	-846
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-22	-11297	-6105	-732	-1329	-2220	-349	*	*											
85	-125	-2093	487	-3425	1176	2162	535	-1429	-1319	-624	-560	403	1575	-833	-1433	-1875	-1439	-3085	307	-847
	206	979	-178	352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-7	-11297	-7830	-732	-1329	-2220	-349	*	*											
86	-805	-2108	209	-1677	375	707	1292	-2814	-2650	1163	-2089	-1009	2100	-1247	-145	-3141	-575	-2100	-3342	890
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-13	-11314	-6864	-732	-1329	-2373	-309	*	*											
87	1027	-1126	60	-1014	-3118	-609	510	-1371	-1340	1592	-2082	-3247	828	-3155	-655	748	185	-594	2061	416
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-47	-11309	-4984	-732	-1329	-2459	-290	*	*											
88	1010	-2062	2035	-781	644	1112	-253	-898	-1068	-267	-3718	-62	-273	343	-18	-986	-508	-1108	354	-296
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-	-1	-11170	-12170	-732	-1329	-3645	-120	*	*	*	*	*	*	*	*	*	*	*	*	*
137	1861	-1980	-235	-180	-422	-564	648	-1013	1885	-1161	-3636	-3123	-2918	236	-1320	-641	-1866	-738	-3214	115
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-	-64	-11170	-4543	-732	-1329	-2534	-274	*	*	*	*	*	*	*	*	*	*	*	*	*
138	2132	-1971	350	-1536	331	-249	-2365	-1236	572	-479	470	-398	-1380	-1598	-3285	-969	-140	354	-3205	-3047
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-	-1	-11160	-12160	-732	-1329	-1629	-563	*	*	*	*	*	*	*	*	*	*	*	*	*
139	565	-2056	27	-924	-1083	80	-2450	-1096	1017	-49	-3712	-3200	-2995	1166	-1412	142	-1596	1864	-3290	-3132
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-	-1	-11256	-12256	-732	-1329	-2581	-264	*	*	*	*	*	*	*	*	*	*	*	*	*
140	-682	1303	422	-907	-282	-126	1486	-733	925	-186	-3723	-2363	-1106	2642	-2541	-289	-533	-323	-3301	-3143
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-	-1	-11268	-12268	-732	-1329	-2260	-338	*	*	*	*	*	*	*	*	*	*	*	*	*
141	660	-2094	539	-290	-321	98	-1511	-952	-26	-419	-3750	-1272	1309	2150	-1648	-1031	-1458	248	-3328	-3170
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-	-7	-11299	-7805	-732	-1329	-3002	-192	*	*	*	*	*	*	*	*	*	*	*	*	*
142	-1082	-2089	2039	-497	-3104	1053	-1505	-306	-465	-1292	-3745	-1458	2107	-2251	-1181	-1697	-1455	489	3323	-866
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-	-24	-11293	-5974	-732	-1329	-2124	-376	*	*	*	*	*	*	*	*	*	*	*	*	*
143	-160	-2082	2008	-2692	-3097	2000	-525	104	-2139	-899	-3738	347	-506	-825	-747	-1947	733	228	1294	3158
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-	-1	-11285	-12285	-732	-1329	-1540	-608	*	*	*	*	*	*	*	*	*	*	*	*	*
144	231	640	1482	-2737	-3150	2109	-2529	419	-205	1185	-3791	-3278	-1343	-507	-92	-1509	-761	-519	-3369	-3211
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-	-62	-11344	4588	-732	-1329	-2172	-362	*	*	*	*	*	*	*	*	*	*	*	*	*
145	1236	-2079	3237	-2697	172	-56	-2474	730	-2621	1685	-533	-1226	-1014	-148	-2565	-477	-3032	790	-3313	-3155
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-	-25	-11281	-5912	-732	-1329	-1517	-620	*	*	*	*	*	*	*	*	*	*	*	*	*
146	1831	70	-3276	-3450	863	-583	-330	905	-675	-172	-3774	-124	-3057	-3170	-1379	-304	-3071	1460	-3352	-879
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147	459	-2140	1485	-990	184	-567	-82	989	-708	451	-3796	-1315	-3079	-353	-3454	-1744	-2455	2413	-3374	-2154
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148	160	-2140	3298	217	-364	1613	-2534	-154	-708	1524	168	-693	-3079	-3192	-1498	-1245	-977	109	238	-3216
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150	-171	-2140	3298	-447	2074	460	-2534	2232	-1381	-102	-2115	-3284	-1346	5	-1498	-3173	-764	525	-3374	-3216
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151	-542	-1145	-169	194	2539	1671	-2512	-674	-1350	1250	1947	-1282	-772	199	-3432	-3152	-730	-696	-3352	-3194
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153	-1314	-2017	-2445	190	532	-757	-178	588	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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-	-1	-11208	-12208	-732	-1329	-1479	-641	*	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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155	61	-1979	96	-297	678	2115	-2373	-1535	-128	-1845	-3635	850	475	110	-3293	-179	-2290	-1149	-3213	144	-97
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162	-381	-2091	-1416	-1646	353	-2698	-2485	-3705	894	1671	-3746	-983	239	2297	-1167	-1087	-3043	-367	-3325	-502	-97
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167	1068	-2072	2181	138	-2245	-2679	-535	-882	431	-871	-3728	-738	-1245	378	-3386	-915	592	522	-3306	-3148	-97
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170	179	-2072	1748	-54	-1066	-438	8	-1711	567	-1086	2078	-955	269	-70	-3366	1078	566	777	3306	807
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171	-407	-2096	-601	374	222	-1081	-2490	1750	171	-1014	-2090	-1488	-3034	-1732	-1037	1894	-549	-683	-3330	-843
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172	-1646	-1139	559	40	-2271	-758	-2507	2069	1706	-1040	-3769	-44	-2341	349	341	-203	-1226	-407	-3347	-173
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173	-803	-2135	-1482	3466	-199	-103	-79	-1407	2110	-1532	-626	-348	458	-1752	-918	457	1592	-461	-3369	-789
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174	94	36	707	-748	-544	-843	424	-159	1786	-484	-3796	-3284	-1887	-1164	-480	-762	1944	-716	-3374	62
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175	69	-2140	234	885	346	1258	424	-3755	1921	-888	-3796	196	485	-491	-185	-363	-764	-1636	-3374	-3216
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177	-1545	36	1225	-431	184	-355	-2534	-1687	2156	-358	-2115	-156	-581	777	293	834	329	-2544	-3374	-3216
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182	-479	807	964	-1646	177	-642	210	-3705	-603	280	-3746	1607	-974	-1726	-373	-346	1931	-1568	-3325	-3167
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183	-992	-570	1224	-1888	2342	-800	261	-1653	-2660	-753	-3774	2012	913	-1131	-1465	-217	-407	-1171	-3352	-3194
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	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-24	-11325	-5982	-732	-1329	-2587	-263		*											
224	-1617	-2096	-3253	-876	95	-1260	764	550	-701	105	-556	-1248	-982	830	-3410	1439	-873	1745	-3330	-931
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-1	-11299	-12299	-732	-1329	-2696	-242		*											
225	-1231	-2096	-2505	-1497	-3111	-2703	32	-1298	-920	36	219	-987	-779	346	-472	2616	-607	-1411	311	797
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-24	-11299	-5939	-732	-1329	-2696	-242		*											
226	-1538	-2072	832	1348	814	-2679	-259	-3687	-1048	-684	-3728	-1212	-971	1043	48	1909	-1170	-2082	-3306	-305
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-7	11272	-7829	-732	-1329	-2221	-348		*											
227	305	-2091	-351	1627	-1099	-1036	-221	-3705	-291	-660	-247	-2394	-509	2358	-111	242	-1644	-805	-3325	-502
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-31	-11294	-5607	-732	-1329	-2786	-226		*											
228	-1578	146	-3220	-337	-1060	-1426	278	-2234	-139	878	1511	-3206	-1239	3002	-584	-101	-3015	-494	-3296	-802
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-25	-11261	-5889	-732	-1329	-2368	-311		*											
229	358	197	-594	428	570	-2228	-2456	-1056	-184	582	-2064	-3206	-1239	1494	239	19	-3015	1532	961	3138
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-38	11261	5301	-732	-1329	-2961	-198		*											
230	-1313	-2027	2444	1093	-3043	-2635	83	-2753	1373	1815	-3	784	-425	733	-540	182	-654	-1489	-455	3103
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-1	-11222	12222	-732	-1329	-3182	-168		*											
231	-623	189	1089	788	2147	-725	625	-3642	1764	437	-3683	-3171	-2966	-3079	-237	-1379	-748	211	-1262	-3103
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-52	-11222	-4845	-732	-1329	-3182	-168		*											
232	-679	-1975	3133	1254	2691	-646	-2369	-3589	-477	-167	-3631	172	-2914	-3027	1977	-264	-85	-139	-1237	-213
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	-52	-11161	4849	-732	-1329	-2453	-291		*											
233	-72	257	-3116	-705	113	504	-2353	-3573	-359	-630	-79	-430	-1098	-1635	2266	1416	47	-2950	-3192	-3034
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-85	-11142	4134	-732	-1329	-2991	-194		*											
234	-571	428	-3030	771	-2887	-2479	-1368	-3486	1724	1507	-1958	-183	-966	-1211	-368	262	-1247	-890	-3106	409
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	-32	-11037	5530	-732	-1329	-2519	-277		*											
235	-493	275	-273	283	-66	-1212	-2298	-3519	347	1911	-3560	942	-232	-1609	-2434	-292	-1173	-678	-3138	-706
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	-75	-11076	4320	-732	-1329	-3463	-137		*											
236	-366	344	-833	-627	1233	-1114	-2222	-357	-781	-191	-1926	2291	-910	-2880	-1508	770	-536	334	-3062	-25
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-8	-10985	-7703	-732	-1329	-2386	-306		*											
237	-1376	364	-3065	-613	2432	-150	878	-1120	-1075	-516	1007	1502	-2846	-2959	-361	521	389	-1324	-3141	-397
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-116	-11081	-3708	-732	-1329	-2142	-371		*											
238	417	-1876	1189	-99	-2891	66	543	-3491	-578	-715	1189	2446	-232	-959	-3190	-609	33	67	596	263

239	-1639	-1912	339	1557	2927	1714	1171	-3527	847	-1727	-165	691	-1065	-415	-1897	-621	-212	-950	-3146	-2988
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-40	-11090	-5231	-732	-1329	-2114	-379	*	*	*	*	*	*	*	*	*	*	*	*	*
240	-1657	-1913	171	2040	862	926	-822	-3527	-1131	-1517	-3569	1257	236	549	-134	47	-1204	-607	-3147	-2989
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241	-2	793	81	1349	-861	1888	-2295	-3515	-2442	-2569	-307	1023	-266	349	-1190	-613	-2853	-170	562	-1962
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-111	-11076	-3763	-732	-1329	-2107	-381	*	*	*	*	*	*	*	*	*	*	*	*	*
242	-1050	270	102	1918	-2924	-1215	821	-3523	-333	-1765	-393	943	1405	481	405	-2390	-817	317	-3143	-2985
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	94	-11091	-3997	-732	-1329	-3646	-120	*	*	*	*	*	*	*	*	*	*	*	*	*
243	-2149	337	296	1325	-1985	-2442	-1250	-3449	-1227	-1038	-328	-50	2802	-863	-927	-537	-2148	11	538	-220
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-111	-11007	-3765	-732	-1329	-3312	-153	*	*	*	*	*	*	*	*	*	*	*	*	*
244	72	831	-1170	2120	-856	106	1502	-3388	-1806	-1287	17	123	-105	-2825	117	-1251	-48	601	-3007	-2849
-	206	979	-180	-352	-37	372	585	-636	438	-131	-675	-164	43	-70	-333	-55	25	-12	-256	-97
-	-5338	-641	-1583	-22	-6015	-2367	-311	*	*	*	*	*	*	*	*	*	*	*	*	*
245	467	1281	-542	-666	-2362	-1954	231	-1088	407	-172	-64	273	2080	181	-989	-719	258	-706	-2581	-323
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-	-28	-10434	-5742	-732	-1329	-2458	-290	*	*	*	*	*	*	*	*	*	*	*	*	*
246	124	-1550	114	751	-2565	-1663	1933	-2178	-1555	-84	230	565	-1208	78	-722	-734	-376	1514	657	-123
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-32	-10679	-5562	-732	-1329	-846	-1173	*	*	*	*	*	*	*	*	*	*	*	*	*
247	-752	-1001	-205	1795	-3009	45	51	-1376	-71	119	336	122	1441	-1039	-574	-1615	-2299	-636	359	386
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-	-1	-11187	-12187	-732	-1329	-2040	-402	*	*	*	*	*	*	*	*	*	*	*	*	*
248	-868	-2038	-543	-92	-3053	-677	-263	751	-2089	1251	2425	410	-185	481	-86	-1412	-602	-757	-3272	-692
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-7	-11237	-7742	-732	-1329	-1941	-435	*	*	*	*	*	*	*	*	*	*	*	*	*
249	-802	-2065	-1401	-3396	-2223	-2224	-1	-731	-1467	-463	3122	705	458	927	743	-2548	-197	832	33	806
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-1	-11266	-12266	-732	-1329	-2262	-337	*	*	*	*	*	*	*	*	*	*	*	*	*
250	-923	84	848	-779	-3108	-594	1658	-1364	-469	-1103	-2068	1236	76	368	699	-936	-647	1624	-3327	-3169
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-1	-11297	-12297	-732	-1329	-3004	-192	*	*	*	*	*	*	*	*	*	*	*	*	*
251	-2408	-2093	2057	-3424	-1241	-2700	579	-1639	-1779	-1291	-3748	2535	267	680	443	-1697	-819	-84	1226	-993
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-1	-11297	-12297	-732	-1329	-2306	-326	*	*	*	*	*	*	*	*	*	*	*	*	*
252	-2420	-2103	-2008	-3434	-861	-2710	265	-1727	-666	-1958	-586	2831	1089	-310	475	-999	-614	-290	2834	929
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-	-24	-11309	-5975	-732	-1329	-2855	-215	*	*	*	*	*	*	*	*	*	*	*	*	*
253	-813	-2080	-3238	-3412	398	-2242	54	-1610	-672	-387	-3736	505	-5	516	2255	-3114	-1044	-332	3768	488
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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254	-2830	149	-3215	-3388	-66	-1422	65	-3671	-137	-1228	-3713	1105	2042	-237	2532	-216	-1504	-868	356	-3133
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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255	68	249	-3121	-710	-104	-628	108	-1684	-332	-646	-3619	-824	2853	328	716	-1297	-61	-1999	-3197	-3039
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256	.57	-11147	4719	.732	-1329	-2738	-234	*	-1461	-452	*	-138	-207	345	2285	562	-744	-242	491	3153	162
	1402	-1935	3022	3256	-2950	1254	-66	-1461	-452	*	-138	-207	345	2285	562	-744	-242	491	3153	162	
	206	979	-178	352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	97	
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257	-2708	-1935	-1195	-3266	-130	-1442	-2329	24	363	-1109	3590	409	1819	3029	199	-2451	-1218	-1354	551	3010	
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259	32	-1838	-2995	-567	-2073	-2042	850	-3452	1578	1601	-3494	366	60	-2890	683	-480	-702	-604	-3072	-2914	
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	-67	-10995	-4469	-732	-1329	-3582	-126	*	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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-	-3	-9735	-10735	-732	-1329	-3920	-99	*	*											
52	-289	137	440	-429	-1245	-1425	-1212	1239	-34	265	-569	396	369	-659	-16	-1851	-269	953	-2052	-89
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57	-172	-619	1279	-377	186	-1077	-1014	3	-313	-1034	-1877	1066	480	-330	-381	-345	649	640	-1854	-1695
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62	-542	-412	886	26	304	-988	-806	-196	-483	-446	978	-1275	1877	-515	-1349	270	-653	185	-1646	-841
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65	-379	-251	636	-1582	607	-858	-645	882	-303	-303	-1907	59	65	-1303	-938	-636	-208	1745	-1485	-1327
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66	-886	-183	-1213	-221	-647	-790	-161	-915	239	352	-1839	1571	-1122	594	683	-954	492	727	-1417	-444
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-	-438	-7805	-1957	-732	-1329	-5702	-28	*	*	-804	-352	-1164	-651	-446	818	81	-541	-149	240	970	
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-	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
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//

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LENG 79			
ALPH Amino			
RF no			
CS no			
COM [converted from an old Plan9 HMM]			
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DATE Mon Mar 8 11:43:15 1999			
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NULT	-4	-8455	
NULE	595	-1558	85 338 -294 -8455
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m->m m->i m->d i->m i->i d->m d->d b->m m->e			
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-	206	979	-179
-	-3259	-161	-9859
2	123	-338	248
-	206	979	-178
-	-4	-9055	-10055
3	294	-360	298
-	206	979	-179
-	-3490	-136	-10090
4	-510	-433	736
-	206	979	-178
-	-60	-9201	-4681
5	-1108	-395	-1552
-	206	979	-178
-	-4	-9143	-10143
6	-205	-454	-485
-	206	979	-178
-	-4	-9234	-10234
7	-1276	-503	134
-	205	979	-176
-	-3707	-116	-10307
8	-359	-475	1207
-	206	979	-178
-	-4	-9265	-10265
9	-20	-542	726
-	206	979	-178
-	-3	-9365	-10365

NY02:195633.1

10	-598	-542	1430	-1874	-182	261	-511	-2073	282	-372	-777	1149	499	371	-1856	-1003	529	317	-1776	19
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-	-3765	-111	-10365	-42	-5127	-4964	-47	*	*	*	*	*	*	*	*	*	*	*	*	*
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18	-396	-598	-209	249	-1613	677	-279	-165	257	211	-50	-1742	-133	-783	1382	-655	333	57	-1832	-1674
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21	-225	-654	-487	271	-139	-304	652	335	-189	-1763	-2309	288	419	-830	1052	538	-1044	901	-1888	-878
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-	-39	-9526	-5289	-732	-1329	-4526	-64	*	*	*	*	*	*	*	*	*	*	*	*	*
22	-537	-657	-157	1082	648	-998	-354	-481	770	-194	-2190	158	437	674	-1388	-775	897	-473	-1891	-1665
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-	-81	-9531	-4236	-732	-1329	-4117	-86	*	*	*	*	*	*	*	*	*	*	*	*	*
23	-936	-661	5	-1422	409	-608	252	-363	29	-92	-796	403	900	1083	25	-28	559	55	-128	-953
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-104	-9537	-3874	-732	-1329	-3502	-133	*	*	*	*	*	*	*	*	*	*	*	*	*
24	-736	46	379	267	950	296	279	424	572	-331	-2331	-159	-1371	934	561	-829	-986	-57	-1909	-1751
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-	-3	-9553	-10553	-732	-1329	-3494	-134	*	-630	*	-482	-647	33	252	339	680	-571	733	-52	-1999	641
25	-862	-765	757	-103	407	-276	-615	-57	-635	-57	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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26	-1526	-753	-143	400	1231	-204	1618	-438	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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-	-129	-9660	-3563	-732	-1329	-3973	-95	438	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
27	-794	-696	1540	423	-1711	-976	-492	*	1436	-1207	-1104	-640	202	-51	-901	528	-82	1001	-271	-2035	671
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-	-3	-9581	-10581	-732	-1329	-3282	-157	*	302	651	-540	-2456	651	-910	-1853	598	-633	490	78	-2035	-1877
28	-731	-801	288	-5	-1064	-558	143	-97	-2365	-97	-414	629	-190	403	-68	-1425	477	984	118	-1985	-1827
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-	-3	-9725	-10725	-732	-1329	-4450	-68	*	1053	-1040	-462	-2355	-315	-1638	-25	-568	336	658	40	-1934	106
29	-777	-801	182	1268	-173	-178	-1147	438	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	206	979	-178	-352	-36	372	585	*	671	-205	342	-1957	-1206	-1714	1310	12	-701	553	-478	-2009	1069
-	-69	-9725	-4461	-732	-1329	-4450	-68	651	-2365	-97	-414	629	-190	403	-68	-1425	477	984	118	-1985	-1827
30	636	-751	-512	97	198	187	-1145	-97	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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31	578	-700	-1411	514	-1342	638	-1094	438	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	206	979	-178	-352	-36	372	585	*	671	-205	342	-1957	-1206	-1714	1310	12	-701	553	-478	-2009	1069
-	-42	-9587	-5173	-732	-1329	-3125	-176	651	-2365	-97	-414	629	-190	403	-68	-1425	477	984	118	-1985	-1827
32	-1286	-775	-159	94	-883	339	677	-97	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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33	437	-775	793	-55	-1791	732	-1170	-772	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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34	-1082	-775	12	-38	-1153	-1155	-345	481	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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35	-96	-775	224	40	-1514	-210	-1170	-82	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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-	-3	-9728	-10728	-732	-1329	-4248	-78	*	332	-314	577	-2458	-384	693	-740	-471	-1126	207	476	-2037	-1878
37	369	-803	-897	893	-1167	-244	403	-314	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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-	-18	-9728	-6438	-732	-1329	-3886	-101	*	7	588	219	-677	-164	41	-73	-335	-54	27	-12	-255	-97
38	391	-806	169	-1716	-103	-229	-1200	7	-1149	953	588	219	-677	-164	41	-73	-335	558	-532	-2040	-1158
-	206	979	-178	-352	-36	372	585	438	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-49	-9732	-4964	-732	-1329	-3907	-100	*	558	-498	705	-425	517	669	504	230	-250	-300	-261	-2017	671
39	-307	-783	458	-1517	-1799	-1341	-2	-498	558	-498	705	-425	517	669	504	230	-250	-300	-261	-2017	671

-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-46	-9702	-5048	-732	-1329	-3638	-121	*	*											
40	50	-786	1003	109	-1801	-426	54	240	-651	-53	-2442	-1008	236	-1838	1520	304	-1323	429	-2020	-1862
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-13	-9705	-7013	-732	-1329	-3668	-118	*	*											
41	183	-810	-742	1011	-731	334	-404	-928	-942	650	-2466	-642	-1206	-122	903	-1843	-285	583	-181	518
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-78	-9738	-4286	-732	-1329	-4247	-78	*	*											
42	-75	-754	1094	476	-1769	-500	-203	-21	-1295	-1814	-2410	427	-511	228	853	818	591	-36	-1988	-1830
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-	-194	-9661	-3003	-732	-1329	-3478	-136	*	*											
43	681	-676	620	490	-1319	-627	-137	-1627	-250	-137	-1056	313	-38	-201	1005	-896	516	-721	-1910	505
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-77	-9553	-4305	-732	-1329	-2989	-194	*	*											
44	210	-763	-892	983	-1778	77	-1157	1046	-1125	-662	-412	790	-771	984	-485	-971	87	601	-1997	-1839
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-80	-9675	-4254	-732	-1329	-3369	-147	*	*											
45	-219	-766	-596	135	-652	397	-803	1168	208	-647	-2422	143	-2	-56	2	-371	871	-475	927	-1842
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-	-61	-9679	-4629	-732	-1329	-3690	-116	*	*											
46	-545	-192	468	-562	-1470	344	995	-2038	-1190	154	942	23	-1466	881	-83	-576	387	968	-489	118
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-42	-9663	-5177	-732	-1329	-3620	-122	*	*											
47	-553	-770	-687	-490	-1464	-1282	1037	796	-900	-382	-1748	233	393	1380	-1037	-730	338	1258	-1456	208
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-11	-9685	-7306	-732	-1329	-3640	-121	*	*											
48	-249	-801	1173	215	-935	-507	402	-244	-1342	366	-2334	706	343	-6	-2065	-750	-192	452	-1819	975
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-19	-9727	-6352	-732	-1329	-4033	-91	*	*											
49	-96	-793	1036	-666	-112	-1381	431	-1079	-250	-1178	357	934	-1198	-594	98	-383	386	1436	-2028	-187
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-20	-9716	-6290	-732	-1329	-3835	-105	*	*											
50	-530	-796	-1474	-158	-632	-397	-306	143	-451	117	-1431	1265	-430	-345	-963	-124	210	1212	-1882	858
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-16	-9720	-6619	-732	-1329	-3672	-118	*	*											
51	-733	-807	872	151	-609	-831	-1202	512	-1085	174	-1417	315	265	-118	588	-1327	680	830	-2042	-1883
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-	-3	-9735	-10735	-732	-1329	-3920	-99	*	*											
52	-289	137	440	-429	-1245	-1425	-1212	1239	-34	265	-569	396	369	-659	-16	-1851	-269	953	-2052	-89
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-3	-9749	-10749	-732	-1329	-4103	-87	*	*											
53	-55	947	236	380	-588	-389	-213	41	-361	-540	-323	1115	219	-174	-711	-495	662	403	-2052	-1894
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54	159	-751	289	572	77	-55	-1145	105	-1292	-296	-2407	774	1059	-615	-509	-669	-481	876	-1985	-1827
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-	-64	-9658	-4566	-732	-1329	-4532	-64	*	*	*	*	*	*	*	*	*	*	*	*	*
55	-100	-705	-318	-214	-883	-598	-538	263	-101	33	-907	1116	922	-114	-334	25	135	404	-1939	-1530
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56	381	44	1665	302	216	-653	-941	-1411	74	-621	-1801	887	-678	-512	-1461	-755	766	80	-1916	-1758
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-	-89	-9562	-4092	-732	-1329	-4716	-56	*	*	*	*	*	*	*	*	*	*	*	*	*
57	-172	-619	1279	-377	186	-1077	-1014	3	-313	-1034	-1877	1066	480	-330	-381	-345	649	640	-1854	-1695
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-	-113	-9474	-3759	-732	-1329	-4259	-77	*	*	*	*	*	*	*	*	*	*	*	*	*
58	124	-583	405	-1093	-1552	109	-977	109	563	-1050	-2238	2002	686	-1084	-756	-523	-53	121	-1817	-897
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-	-45	-9421	-5099	-732	-1329	-4991	-46	*	*	*	*	*	*	*	*	*	*	*	*	*
59	12	-553	1111	-1011	-1	-252	-764	-1203	189	-1388	-916	989	1288	-411	-829	-619	692	-192	-1787	458
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-	-54	-9379	-4829	-732	-1329	-4725	-56	*	*	*	*	*	*	*	*	*	*	*	*	*
60	-391	-531	230	-158	63	80	360	691	-984	-484	-2187	1022	1232	-1090	-1776	-602	518	426	-1765	-1607
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61	233	-449	-245	433	1122	-969	54	-1251	-306	-638	-1112	819	-494	209	-89	-209	820	177	-1338	-302
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-105	-9225	-3861	-732	-1329	-4698	-57	*	*	*	*	*	*	*	*	*	*	*	*	*
62	-542	-412	886	26	304	-988	-806	-196	-483	-446	978	-1275	1877	-515	-1349	270	-653	185	-1646	-841
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-81	-9169	-4247	-732	-1329	-4674	-58	*	*	*	*	*	*	*	*	*	*	*	*	*
63	-577	714	-1482	-842	-821	-986	87	297	561	-105	-2035	867	371	-1431	-849	-558	973	1284	-1613	-652
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-	-30	-9118	-5732	-732	-1329	-5214	-39	*	*	*	*	*	*	*	*	*	*	*	*	*
64	-218	-362	591	-710	1123	-969	-537	305	940	-59	-2017	894	-823	-248	532	-818	-630	-89	-456	-1110
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-	-175	-9090	-3155	-732	-1329	-5239	-39	*	*	*	*	*	*	*	*	*	*	*	*	*
65	-379	-251	636	-1582	607	-858	-645	882	-303	-303	-1907	59	65	-1303	-938	-636	-208	1745	-1485	-1327
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-	-113	-8912	-3777	-732	-1329	-5382	-35	*	*	*	*	*	*	*	*	*	*	*	*	*
66	-886	-183	-1213	-221	-647	-790	-161	-915	239	352	-1839	1571	-1122	594	683	-954	492	727	-1417	-444
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-	-5	-8801	-9801	-732	-1329	-5421	-34	*	*	*	*	*	*	*	*	*	*	*	*	*
67	-353	-27	1175	-1514	276	-790	-577	958	125	110	-1839	-1327	632	-1235	-1497	-567	-137	1162	-1417	-1259
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-	-82	-8801	-4232	-732	-1329	-5421	-34	*	*	*	*	*	*	*	*	*	*	*	*	*
68	-879	-136	740	-234	146	-743	668	128	-154	83	-1791	949	696	-126	-1055	-1115	348	666	-1370	-1212
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97

-	-5	-8719	-9719	-732	-1329	-5443	-34	*	177	-616	-1313	614	336	-58	-1450	-1169	-1088	1457	-1370	-1212
69	-506	-136	1261	-117	-76	-440	-530	9	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	206	979	-178	-352	-36	372	585	-635	*	*	*	*	*	*	*	*	*	*	*	*
-	-109	-8719	-3824	-732	-1329	-5443	-34	*	-592	-671	-1149	974	677	-979	-1388	-279	72	670	-1308	-1149
70	38	-73	1252	-672	468	-406	133	-263	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	206	979	-178	-352	-36	372	585	-635	*	*	*	*	*	*	*	*	*	*	*	*
-	-103	-8610	-3914	-732	-1329	-5476	-33	*	-558	-1126	-1673	2130	-956	-1069	292	-1050	-970	388	-1251	-1093
71	-790	-17	2062	-696	-1032	-624	-411	-867	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	206	979	-178	-352	-36	372	585	-635	*	*	*	*	*	*	*	*	*	*	*	*
-	-6	-8506	-9506	-732	-1329	-5497	-32	*	-325	-1066	-1673	1683	218	137	-1331	-677	-204	-418	-1251	-1093
72	175	-17	1314	-452	913	-624	-411	-179	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	206	979	-178	-352	-36	372	585	-635	*	*	*	*	*	*	*	*	*	*	*	*
-	-162	-8506	-3271	-732	-1329	-5497	-32	*	-471	-553	-1585	2472	1258	-981	-1058	-241	-882	-921	-1163	-1005
73	-379	71	849	-780	-675	-536	-5	-1544	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	206	979	-178	-352	-36	372	585	-635	*	*	*	*	*	*	*	*	*	*	*	*
-	-7	-8338	-9338	-732	-1329	-5530	-32	*	188	-1039	-1585	732	1809	-981	-244	-962	-882	-921	-1163	-1005
74	-33	71	1534	73	-944	-536	806	-1282	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	206	979	-178	-352	-36	372	585	-635	*	*	*	*	*	*	*	*	*	*	*	*
-	-7	-8338	-9338	-732	-1329	-5530	-32	*	-471	-1039	-1585	1561	1660	-328	58	-713	-132	-680	-1163	-1005
75	-331	71	1087	-654	975	275	464	-801	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	206	979	-178	-352	-36	372	585	-635	*	*	*	*	*	*	*	*	*	*	*	*
-	-216	-8338	-2878	-732	-1329	-5530	-32	*	499	-446	-1477	-965	1226	2	-232	155	-329	-768	-1055	-897
76	407	179	-935	384	1376	-401	-215	-1380	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	206	979	-178	-352	-36	372	585	-635	*	*	*	*	*	*	*	*	*	*	*	*
-	-304	-8119	-2422	-732	-1329	-5608	-30	*	-225	-793	-1339	-827	2057	-736	-998	-717	472	26	-918	-759
77	-457	316	-841	-1015	1901	-291	-78	-1298	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	206	979	-178	-352	-36	372	585	-635	*	*	*	*	*	*	*	*	*	*	*	*
-	-438	-7805	-1957	-732	-1329	-5702	-28	*	804	-352	-1164	-651	-446	818	81	-541	-149	240	970	-584
78	-281	492	-665	-171	1368	-115	98	-956	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	206	979	-178	-352	-36	372	585	-635	*	*	*	*	*	*	*	*	*	*	*	*
-	-522	-7424	-1749	-732	-1329	-5819	-26	*	125	-443	-990	-477	-272	-386	-648	-367	-286	-325	-568	-410
79	-107	665	-492	-665	2478	59	272	-948	125	-443	-990	-477	-272	-386	-648	-367	-286	-325	-568	-410
-	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
-	*	*	*	*	*	*	*	*	0	*	*	*	*	*	*	*	*	*	*	*

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10	-97	-765	-1923	1931	-1780	-1372	-1159	-2379	889	-205	-2421	834	-1704	462	-2079	42	1031	-633	-1999	-1841
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-3	-9703	-10703	-732	-1329	-76	-4293	*	*											
11	678	-765	-1923	1499	19	-1372	-1159	-1003	639	-1874	2448	155	-1704	-338	-1047	255	-862	-1756	-1999	926
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-134	-9703	-3516	-732	-1329	-76	-4293	*	*											
12	-210	-668	-1826	1622	-1683	-1275	-1062	-2283	985	966	-123	551	-1607	-1720	-1982	656	-1621	218	-1902	-1744
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-3	-9571	-10571	-732	-1329	-1349	-719	*	*											
13	206	-668	-1826	1035	-1683	-656	-1062	-2283	1500	-1777	-2324	1789	-1607	352	0	769	-299	-1659	-1902	-1744
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-67	-9571	-4507	-732	-1329	-1349	-719	*	*											
14	-400	-622	-1779	214	-1637	-1229	-1016	-2236	1435	18	-2277	1511	-1560	707	-1936	1176	-1574	566	-1856	-1698
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-3	-9507	-10507	-732	-1329	-371	-2140	*	*											
15	-1495	-722	191	1199	-1737	-1329	-1116	0	992	53	-2377	622	-1660	1106	-253	-268	276	167	-1956	-1798
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-3	-9645	-10645	-732	-1329	-805	-1226	*	*											
16	-334	-722	-1879	-2053	-1737	-1329	-1116	-1221	1902	722	-1115	1658	-1660	-460	355	219	-85	-931	-1956	-1798
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-3	-9645	-10645	-732	-1329	-45	-5022	*	*											
17	-95	-765	273	1474	-1780	-1372	-1159	-2379	-1306	-1874	-2421	93	-1704	2190	1291	296	346	-1756	-1999	-1841
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-3	-9703	-10703	-732	-1329	-76	-4293	*	*											
18	-1538	1686	1504	-1195	-1780	-1372	-1159	-1003	178	1021	522	656	-1704	735	-2079	1006	-862	-1756	-1999	-1841
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-3	-9703	-10703	-732	-1329	-76	-4293	*	*											
19	-702	-765	391	1171	-1780	-1372	-1159	-2379	353	1472	75	-437	-1704	1354	-2079	468	-1717	-1756	-1999	-1841
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-3	-9703	-10703	-732	-1329	-76	-4293	*	*											
20	-1538	-765	1375	54	-1780	475	-1159	-2379	510	613	-2421	760	-1704	1066	343	580	-1525	-1756	-1999	-1841
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-3	-9703	-10703	-732	-1329	-76	-4293	*	*											
21	501	-765	-699	623	-1780	-1372	-1159	-2379	211	1217	-2421	155	-1704	1550	-185	800	-1717	-1756	-1999	-1841
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-3	-9703	-10703	-732	-1329	-76	-4293	*	*											
22	-305	-765	1108	1232	-1780	-1372	1076	476	-1306	-273	-2421	-126	-1704	986	842	509	-843	-1756	-1999	-1841
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-3	-9703	-10703	-732	-1329	-76	-4293	*	*											
23	555	-765	-1923	1559	-1780	-1372	-1159	-40	-1306	884	-2421	1213	-1704	478	-460	-283	271	-1756	-1999	-1841
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-3	-9703	-10703	-732	-1329	-76	-4293	*	*											
24	-1538	-765	1324	2246	-1780	56	269	-2379	-1306	-1874	-2421	324	-1704	547	-308	655	-564	-1756	-1999	-1841
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97

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-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-153	-9599	-3328	-732	-1329	-1150	-864	*	*											
40	-612	-575	-1733	724	-1590	-288	-969	229	1435	1452	241	-1718	-1514	-1627	-995	419	-1527	-1311	-1809	-1651
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-3	-9433	-10433	-732	-1329	-1874	-459	*	*											
41	-1348	1135	330	661	-1590	-1182	613	-2189	45	446	-2231	1139	-1514	2104	937	-1453	-875	-1566	-1809	-1651
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-3	-9433	-10433	-732	-1329	-1874	-459	*	*											
42	806	-575	733	608	-1590	-329	-969	-2189	-115	925	-474	509	-1514	821	-875	-181	-1527	-315	-1809	-1651
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-3	-9433	-10433	-732	-1329	-1874	-459	*	*											
43	-114	789	-451	876	-1590	-1182	62	-2189	-1116	1080	-2231	-434	-1514	2299	-218	-167	-1527	-529	-1809	-1651
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-113	-9433	-3756	-732	-1329	-1874	-459	*	*											
44	952	-496	542	-1828	-1512	-401	-891	688	1013	814	1187	-253	-1435	-1548	-542	-779	-1449	-237	-1730	-1572
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-146	-9313	-3401	-732	-1329	-2208	-352	*	*											
45	-1169	-396	943	1796	-1411	-1003	1078	-2010	-57	169	-2051	-343	-1334	94	-1710	845	-1348	126	-1630	-1472
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-4	-9112	-10112	-732	-1329	-2511	-278	*	*											
46	-359	-396	1574	341	-1411	92	-790	-694	-937	560	1027	226	-1334	599	129	-1429	468	-1387	-1630	-1472
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-80	-9112	-4263	-732	-1329	-2511	-278	*	*											
47	-186	-345	-714	2004	74	-952	-739	-1182	70	961	48	-1489	-1284	-1397	-1659	347	-1298	-404	-1579	-1421
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-4	-9038	-10038	-732	-1329	-2664	-248	*	*											
48	25	908	1639	884	-1360	-412	472	-1575	-886	297	-2001	-1489	-1284	1639	180	-664	-880	-1336	-1579	-1421
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-4	-9038	-10038	-732	-1329	-2664	-248	*	*											
49	-498	-345	312	1369	178	994	-739	-1016	-886	33	542	1201	-1284	-1397	168	-398	-1298	-1336	-1579	-1421
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-84	-9038	-4186	-732	-1329	-1978	-422	*	*											
50	271	-346	885	785	-151	-234	-740	-1960	-887	113	-2001	478	179	1231	336	-718	113	-1337	-1580	-1421
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-17	-9041	-6708	-732	-1329	-2719	-238	*	*											
51	-433	-338	-1495	1380	-1353	-945	-732	371	-879	836	255	1009	-1276	-1390	528	265	-1290	-297	-1572	-1413
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-4	-9031	-10031	-732	-1329	-2769	-229	*	*											
52	322	-338	-590	1312	-1353	-945	-732	-1952	-879	225	-1993	-1481	-1276	1292	1048	1164	-1102	-1329	-1572	-1413
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-4	-9031	-10031	-732	-1329	-2001	-415	*	*											
53	-1161	-388	631	1806	-1403	-146	-782	-2003	-929	413	748	-1532	154	840	252	-580	-1341	-131	-1622	-1464
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-286	-9102	-2488	-732	-1329	-2364	-312	*	*											

54	352	-215	-223	1947	-1230	-822	-609	-1830	-756	-1324	313	-1358	113	1015	952	278	-1168	-1206	-1449	-1291
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-301	-8845	-2427	-732	-1329	-2908	-206	*	*	*	*	*	*	*	*	*	*	*	*	*
55	323	-40	1037	1549	-1056	399	-435	-98	142	-1150	-1696	505	-979	341	-1354	-1005	-146	-1032	-1274	-1116
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-548	-8561	-1674	-732	-1329	-3326	-152	*	*	*	*	*	*	*	*	*	*	*	*	*
56	645	250	436	877	-765	164	-144	-1364	-291	183	-1406	-893	-689	470	-110	-594	-703	630	-984	-826
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-9	-7974	-8974	-732	-1329	-3655	-119	*	*	*	*	*	*	*	*	*	*	*	*	*
57	1091	250	-908	418	-765	445	-144	-62	434	24	-1406	-893	-689	96	-1064	158	133	-741	-984	-826
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-63	-7974	-4692	-732	-1329	-3655	-119	*	*	*	*	*	*	*	*	*	*	*	*	*
58	-497	276	228	-315	-739	379	-118	-1339	582	49	-1380	1411	-663	1081	163	-757	58	-715	-958	-800
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-198	-7928	-3011	-732	-1329	-3691	-116	*	*	*	*	*	*	*	*	*	*	*	*	*
59	705	361	-797	326	-654	-246	-33	-920	-181	755	-1295	-783	-578	-691	-953	934	332	-631	-873	-715
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-160	-7709	-3319	-732	-1329	-3759	-111	*	*	*	*	*	*	*	*	*	*	*	*	*
60	187	425	-452	204	-590	424	31	-1189	385	28	-1230	-718	-513	-627	1072	205	448	-566	-809	-650
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-330	-7581	-2328	-732	-1329	-3828	-105	*	*	*	*	*	*	*	*	*	*	*	*	*
61	-226	548	-610	286	-468	-60	153	-1067	6	-406	-1108	-596	-391	1784	-767	1078	-405	-444	-687	-528
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-449	-7247	-1937	-732	-1329	-3913	-99	*	*	*	*	*	*	*	*	*	*	*	*	*
62	653	696	-462	412	-319	89	302	146	155	-239	-960	-447	-242	-356	616	-337	-256	-295	-538	-380
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-19	-6860	-7860	-732	-1329	-4022	-92	*	*	*	*	*	*	*	*	*	*	*	*	*
63	-77	696	-462	390	-319	89	302	-918	155	308	-960	-447	-242	966	-618	-337	671	-295	-538	-380
-	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
-	*	*	*	*	*	*	*	*	0	*	*	*	*	*	*	*	*	*	*	*

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HMMER2.0		NAME acidic.text		DESC		LENG 28		ALPH Amino		RF no		CS no		COM {converted from an old Plan9 HMM}		NSEQ 0		DATE Mon Mar 8 11:40:16 1999		XT -8455 -4 -1000 -1000 -8455 -4 -8455		NULT -4 -8455		NULE 595 -1558 85 338 -294 453 -1158 197 249 902 -1085 -142 -21 -313 45 531 201 384 -1998 -644		HMM		Y											
m->m		m->i		m->d		i->m		i->i		d->m		d->d		b->m		m->e																							
-202		*		-2939		84		-63		345		558		-662		411		-157		-703		-191		14		-100		-362		-81		0		-39		-282		-123	
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2		179		953		-205		-63		345		558		-662		411		-157		-703		-191		14		-100		-362		-81		400		-39		-282		-123	
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4		150		923		-234		-92		316		529		-691		382		-186		-732		-220		-15		-129		137		-110		420		-68		-311		-152	
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-	-36	-5924	-6924	-732	-1329	-1478	-642	*	*	*	*	*	*	*	*	*	*	*	*	*
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-	-36	-5924	-6924	-732	-1329	-1478	-642	*	*	*	*	*	*	*	*	*	*	*	*	*
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-	-36	-5924	-6924	-732	-1329	-1478	-642	*	*	*	*	*	*	*	*	*	*	*	*	*
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-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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-	-36	-5924	-6924	-732	-1329	-1478	-642	*	*	*	*	*	*	*	*	*	*	*	*	*
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-	-36	-5924	-6924	-732	-1329	-1478	-642	*	*	*	*	*	*	*	*	*	*	*	*	*

-	-36	-5924	-6924	-732	-1329	-1478	-642	*	*	-186	-732	-220	-15	-129	-391	-110	-29	-68	-311	529
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-	-763	-8004	-1298	-732	-1329	-2034	-404	*	*											
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-	-14	-7251	-8251	-732	-1329	-2653	-250	*	*											
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-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-14	-7251	-8251	-732	-1329	-2653	-250	*	*											
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-	-14	-7251	-8251	-732	-1329	-2653	-250	*	*											
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-	-14	-7251	-8251	-732	-1329	-2653	-250	*	*											
16	659	2591	-566	-740	-424	-16	1897	-79	50	-518	-1065	-552	-347	-461	-723	-442	-361	143	-643	-485
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-	-14	-7251	-8251	-732	-1329	-2653	-250	*	*											
17	1345	591	-566	518	-424	874	197	-1023	50	-518	-1065	-552	-347	-461	-723	-442	-361	-400	-643	-485
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-	-14	-7251	-8251	-732	-1329	-2653	-250	*	*											
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-	-14	-7251	-8251	-732	-1329	-2653	-250	*	*											
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-	-18	-6891	-7891	-732	-1329	-2810	-222	*	*											
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26	27	800	-192	-71	-215	193	406	-635	438	-130	-856	302	1100	-252	-514	71	-153	-192	-434	-276
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-	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
-	*	*	*	*	*	*	*	*	0	*	*	*	*	*	*	*	*	*	*	*

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10	1318	-1935	340	148	-1357	581	-1091	-86	-690	-381	-254	-57	1369	-368	-566	-247	-3102	-422	-1823	-3765
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15	-1034	-624	386	-20	-2342	1988	33	367	-109	-199	162	-171	-1634	-588	307	-384	-1724	-119	-4884	-4726
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18	-506	83	276	282	-2197	318	1173	365	465	-288	-2944	-87	-1223	932	1004	-387	-1297	332	-4922	-3758
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21	-155	-1092	2375	-419	-1908	-866	129	434	-1201	-111	-1287	96	-1285	-407	-572	-857	-918	776	-1827	-1650
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22	-218	-842	-151	-203	-3056	545	-256	881	-220	-8	-416	346	-2135	-143	634	-724	-637	1158	-375	-1555
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23	-64	-1985	814	-989	-4727	-64	-1586	1888	-593	575	-1209	-108	-2137	44	-976	-1423	-464	933	-1843	-2567
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24	-583	-1822	-527	280	-3015	-1004	-2221	453	-593	1039	-18	700	-3287	-217	309	-150	-503	1325	-1842	-2914
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-	-5	-13022	-8266	-732	-1329	-1746	-511	*	*	122	-922	696	-1366	-127	52	332	-790	933	-2081	-916
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-	-6708	-57	-5109	-4	-8558	-3141	-174	*	*	489	-285	-255	-3379	242	-767	-732	-466	693	-4781	-1155
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-	-50	-12818	-4875	-732	-1329	-4511	-65	*	*	18	-955	-935	-1854	259	504	-702	-632	1243	-1322	-1745
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ALPH Amino		RF no	
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5		308 539 -619 4 539 -69 144 -205 -3 627 -1117 178 445 -513 -776 -495 -414 93 -695 -537	
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8		-289 485 -673 17 -530 -122 91 -710 523 -54 420 717 -454 -567 -829 740 456 7 -749 -591	
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10		-12 -7519 -8519 -732 -1329 -3171 -170 *	
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-	10	7735	-8735	732	1329	-3346	-149	*	*											
38	397	396	683	936	784	-211	1	141	453	-714	-741	-748	-543	-656	61	818	-78	-576	-838	-680
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	12	-255	97
-	-10	7735	-8735	-732	-1329	-3346	-149	*	*											
39	126	396	-89	234	758	-211	1161	-368	299	-158	-1260	-748	-543	-656	-134	164	-557	261	-838	434
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	97
-	-10	-7735	-8735	-732	-1329	-3346	-149	*	*											
40	744	396	-202	-270	-619	-211	1159	-132	216	-284	-1260	60	-543	-656	-918	668	196	48	-838	-680
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	97
-	-10	-7735	-8735	-732	-1329	-3346	-149	*	*											
41	-378	396	153	-936	-619	-211	1	459	865	-714	-1260	785	828	278	411	-638	-557	107	-838	-680
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	97
-	-10	-7735	-8735	-732	-1329	-3346	-149	*	*											
42	169	396	151	-924	852	-211	1028	-1219	997	-714	472	255	-543	-656	469	-638	81	107	-838	-680
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	97
-	-10	-7735	-8735	-732	-1329	-3346	-149	*	*											
43	713	396	-749	1	1185	-111	1	-1219	-146	-201	-1260	-748	-543	-3	252	-638	-379	1006	-838	-680
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	97
-	-10	-7735	-8735	-732	-1329	-3076	-182	*	*											
44	956	369	-788	-207	-646	-238	-25	-1245	1219	-179	-1287	-421	-569	251	-945	-640	528	92	-865	707
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	97
-	-10	-7794	-8794	732	1329	-3313	-153	*	*											
45	627	369	-81	223	646	-238	-25	844	417	69	1287	244	185	-683	945	-664	-583	91	-865	707
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	12	-255	97

46	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	172	389	-1202	242	-569	-340	638	254	-405	87	835	-707
	550	369	13	-962	353	-238	-25	-262	-172	438	-130	-677	-164	41	-73	-335	-54	27	-12	255	97
-	206	979	-178	-352	-36	372	585	-635	*	*	*	*	*	*	*	*	*	*	*	*	*
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*	*
47	148	369	-100	442	-646	495	-25	-1245	771	117	-1287	-730	-730	266	-683	63	-179	-583	359	865	707
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	12	255	97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*	*
48	-404	369	-788	-99	-646	94	-25	310	724	404	-1287	122	-569	-569	132	130	-7	164	-622	865	267
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	255	97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*	*
49	-404	369	-788	-690	-646	171	-25	1063	833	386	-1287	-774	-774	-569	-5	-945	263	-583	-387	865	911
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	255	97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*	*
50	197	1310	-76	-136	198	134	15	-1206	374	-139	-1247	347	-530	-530	-643	-894	28	-544	113	-825	1433
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	255	97
-	-10	-7702	-8702	-732	-1329	-2981	-195	*	*	*	*	*	*	*	*	*	*	*	*	*	*
51	-404	1823	-652	1115	-646	-124	272	-1245	280	-170	-1287	-447	-569	-569	-683	385	-12	-583	-87	865	1131
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	12	255	97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*	*
52	963	369	-788	633	-391	187	-25	385	366	-570	850	-774	-774	-569	-683	-945	-664	-583	390	-865	530
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*	*
53	-404	369	-788	486	-601	187	-25	1072	733	404	-1287	-774	-774	-569	-683	-945	-12	-22	-622	-865	60
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
-	10	7794	8794	732	1329	3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*	*
54	404	369	788	547	816	171	416	629	-172	509	-1287	-18	-18	-569	314	-945	-664	-583	-622	-865	563
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
-	10	7794	8794	732	1329	3313	153	*	*	*	*	*	*	*	*	*	*	*	*	*	*
55	859	369	788	167	646	534	-25	-232	586	-179	-1287	-774	-774	272	-683	-945	-161	-414	-460	-865	1207
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	12	-255	-97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*	*
56	-404	369	-788	-99	1015	-238	-25	176	741	-189	-1287	122	-569	-569	132	-945	-253	623	-622	-865	938
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*	*
57	19	1986	-788	-318	-646	-238	-25	392	1278	-333	-1287	213	-569	-569	-5	-171	-264	176	-622	-865	-707
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*	*
58	-4	1498	-788	-641	-646	-238	1001	442	-165	-169	508	-774	-774	-569	346	964	-7	-583	-78	-865	272
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*	*
59	711	369	-788	-84	262	179	884	-1245	822	-170	621	-774	-774	-569	-683	-945	-7	-22	22	-865	115
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*	*
60	142	369	-788	663	451	-238	-25	-1245	-172	-3	-1287	213	-569	-569	1051	-56	-664	189	80	-865	413
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	-12	-255	-97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*	*
61	379	369	-788	-167	262	495	-25	-870	-172	255	-1287	-774	-774	62	719	-945	319	289	-65	-865	-707
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	-164	41	-73	-335	-54	27	12	-255	-97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*	*
62	717	1285	-788	-732	1329	3313	-153	-160	-159	-184	644	-675	-675	-44	807	-945	-55	114	-87	-865	-707
-	10	7794	8794	732	1329	3313	94	-25	-159	-184	644	-675	-675	-44	807	-945	-55	114	-87	-865	-707

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-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	12	255	-97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*
63	-170	369	-228	655	-646	301	-25	-1245	-172	-740	641	565	-569	-683	434	-383	533	673	-865	-707
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*
64	138	369	-788	422	-646	-238	-25	-1245	-172	355	463	-774	-569	377	839	254	-414	374	-865	-707
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*
65	-4	369	-547	-84	-646	417	-25	-394	-172	333	-1287	1241	-569	375	623	-664	-583	-622	-865	272
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*
66	-404	1506	-788	310	-646	179	1034	-1245	768	-179	-1287	-774	-569	-3	-945	-264	189	346	-865	1258
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*
67	333	369	-788	-962	-646	316	1117	-1245	-172	-740	-1287	849	-569	-683	501	285	543	68	865	845
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-70	-7794	-4535	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*
68	-378	1630	-762	-86	-619	333	285	-407	373	-714	535	1069	-543	172	924	-638	-557	61	-838	680
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-10	-7735	-8735	-732	-1329	-3346	-149	*	*	*	*	*	*	*	*	*	*	*	*	*
69	802	396	67	-664	-619	-211	1	-925	-146	431	1256	9	-543	-656	534	-638	-557	367	-838	680
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-10	-7735	-8735	-732	-1329	-3346	-149	*	*	*	*	*	*	*	*	*	*	*	*	*
70	169	396	312	428	-619	-211	1161	-1219	180	207	1069	-748	-543	-656	-918	14	484	-596	-838	313
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-122	7735	-3714	732	1329	-3346	-149	*	*	*	*	*	*	*	*	*	*	*	*	*
71	331	443	-375	559	-329	390	1206	-433	799	-667	703	-701	655	-610	-872	366	-510	-549	791	-633
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	11	7627	8627	-732	-1329	3132	-175	*	*	*	*	*	*	*	*	*	*	*	*	*
72	289	415	-742	-916	-600	597	21	-1199	-126	650	1291	28	-523	-637	-899	654	-537	68	-819	-661
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-11	-7691	-8691	-732	-1329	-3370	-147	*	*	*	*	*	*	*	*	*	*	*	*	*
73	-341	415	172	-916	-600	225	21	-387	-126	623	1182	-706	-523	-637	88	-568	-537	640	-819	890
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	97
-	-11	-7691	-8691	-732	-1329	-3370	-147	*	*	*	*	*	*	*	*	*	*	*	*	*
74	-358	415	170	-916	-600	-192	21	-240	787	424	691	-489	109	44	-899	300	-537	-32	-819	559
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-11	-7691	-8691	-732	-1329	-3101	-179	*	*	*	*	*	*	*	*	*	*	*	*	*
75	-385	388	-769	343	-627	-219	74	-1226	553	-160	950	585	-550	-664	1117	365	-564	-89	-846	-687
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-10	-7752	-8752	-732	-1329	-3339	-150	*	*	*	*	*	*	*	*	*	*	*	*	*
76	-385	388	-769	1216	378	-219	-6	-1226	-153	-202	-1267	-755	-550	854	-926	300	-564	570	-846	550
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-10	-7752	-8752	-732	-1329	-3339	-150	*	*	*	*	*	*	*	*	*	*	*	*	*
77	162	388	60	518	-627	-219	865	-1226	303	244	-1267	-755	-550	821	430	-645	-564	110	-846	306
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-10	-7752	-8752	-732	-1329	-3339	-150	*	*	*	*	*	*	*	*	*	*	*	*	*
78	385	388	131	569	754	-219	-6	-235	-153	619	-1267	-755	-550	271	-926	12	-564	-390	-846	860
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	97
-	10	-7752	-8752	-732	-1329	3339	-150	*	*	*	*	*	*	*	*	*	*	*	*	*

79	527	388	-769	260	311	115	1501	-155	797	-151	-1267	1	-550	-664	359	-645	-564	603	-846	-687
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	255	97
-	-10	-7752	-8752	-732	-1329	-3133	-1732	*	*	*	*	*	*	*	*	*	*	*	*	*
80	-404	369	-788	320	369	-238	1034	-191	256	116	-1287	-774	-569	377	1028	-664	-583	544	865	707
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*
81	-404	2462	126	-962	-646	-238	1117	-985	366	6	889	-774	-569	375	95	198	-583	-622	865	520
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	255	97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*
82	-404	369	124	-285	119	241	-25	297	417	487	-1287	-774	-569	-683	34	226	-583	-106	-865	520
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*
83	250	369	13	-962	1137	-238	-25	680	-172	-228	-1287	-774	-569	132	41	343	-583	-184	865	564
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	12	255	97
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84	370	369	-788	-112	808	-238	1519	-1245	-172	109	1685	7	-569	-683	-945	-664	-583	74	865	756
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	12	255	-97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*
85	100	1880	13	-962	145	-238	1132	-434	416	451	621	-126	-569	-663	262	-664	-583	-622	865	242
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*
86	148	1431	-788	-106	541	-238	-25	-985	740	54	-1287	-774	-569	345	-945	874	583	143	-865	707
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	255	97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*
87	714	2092	-788	-962	-646	-238	-25	-1245	272	369	867	213	-569	-683	-945	848	-583	-622	-865	707
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	255	97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*
88	-404	1515	754	726	-646	241	-25	-184	190	431	644	-774	-569	-683	-945	-12	-583	-622	865	707
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-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*
89	346	1506	-788	261	-646	-238	-25	-1245	257	750	641	213	-569	105	-945	-186	-414	-1	-865	707
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	255	-97
-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*
90	156	1532	-788	312	-646	-238	-25	710	-172	6	-258	7	-569	-683	41	-664	-583	928	-865	707
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-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*
91	142	2166	-93	-194	-646	-238	-25	545	-172	474	-707	577	-569	-683	-158	-664	-583	22	-865	707
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92	370	1530	-213	214	-646	-238	1001	-1245	191	436	-1287	659	-569	105	-945	-664	-583	495	-865	-707
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93	309	369	13	-84	292	-238	-25	-407	-172	794	-1287	-126	-569	142	-945	56	547	-622	-865	-707
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94	458	369	-788	1045	814	-238	1481	583	-172	-740	-1287	-774	-569	352	-945	-664	164	-622	-865	-707
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-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*
113	-404	1994	-788	-962	-646	-238	1823	-1245	-172	101	-1287	-19	819	-683	420	-161	-583	346	1296	-707
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-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*
114	19	369	-116	-690	-646	-238	-25	315	428	394	-891	-774	-569	-683	417	-664	797	68	1419	-707
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-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*
115	-67	667	-788	207	385	-238	585	816	-172	118	-1287	-774	185	-683	-945	636	542	622	-865	-707
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-	-10	-7794	-8794	-732	-1329	-3313	-153	*	*	*	*	*	*	*	*	*	*	*	*	*
117	-404	1506	-788	-99	120	241	-25	-1245	-172	-126	470	7	292	-5	-945	-664	869	393	1444	-707
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118	539	1243	-788	-962	-646	-238	1101	-158	-172	81	-1287	122	-569	-683	-945	267	-583	438	1441	-707
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119	176	2168	506	-929	153	-205	8	487	440	431	337	-741	-536	-650	-912	-631	-73	-589	-832	673
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120	201	2228	541	134	-613	-205	8	-127	-139	-194	-1253	-741	-536	-650	-912	292	902	589	-832	673
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121	610	403	755	-53	613	204	8	-857	-139	526	-1253	-741	-536	315	-912	-631	41	1104	832	-673
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122	-371	403	-755	936	741	-205	8	-157	-139	-136	-1253	-741	245	394	-912	-631	31	587	-832	320
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123	-332	441	950	-890	364	-166	47	-900	-100	714	-1214	109	352	-611	-873	-79	-34	209	-793	-634
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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126	28	462	-696	-226	1020	-145	1201	-1153	744	-648	-1194	-682	386	468	-852	-160	101	-13	-772	535
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127	375	434	-723	-897	1226	-173	40	241	657	-675	-1221	-709	753	-618	-880	42	-182	-557	-800	595
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128	-671	103	-1055	-1229	445	-504	-291	-91	151	-1007	-1553	-1041	263	-121	-1211	1749	-96	-244	784	1167
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130	-633	140	-1018	-395	154	-467	443	778	-402	-213	-1516	335	-799	-912	-765	1785	-813	-852	-1094	322
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-70	-8278	-4497	-732	-1329	-3042	-187	*	*	*	*	*	*	*	*	*	*	*	*	*
131	-115	173	-276	-294	511	-435	-222	-1442	461	-592	-1483	-35	-766	2557	-1142	-758	-767	-174	-1061	350
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-	-7	-8216	-9216	-732	-1329	-2700	-241	*	*	*	*	*	*	*	*	*	*	*	*	*
132	-504	139	-1019	-423	-876	-468	-255	-1476	196	-971	399	2438	-264	-913	-1175	-381	-722	1231	-1095	-937
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-	-7	-8280	-9280	-732	-1329	-3034	-188	*	*	*	*	*	*	*	*	*	*	*	*	*
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-	-7	-8280	-9280	-732	-1329	-2924	-204	*	*	*	*	*	*	*	*	*	*	*	*	*
134	-643	131	2147	-321	905	-18	1242	205	-411	-979	-1525	-231	-808	-494	-264	-903	-230	-861	-1103	-945
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-7	-8295	-9295	-732	-1329	-3018	-190	*	*	*	*	*	*	*	*	*	*	*	*	*
135	-643	131	494	424	-885	-477	-142	-1484	-411	-556	-1525	-324	28	-921	-188	1922	-822	-145	-1103	-613
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-41	-8295	-5326	-732	-1329	-3018	-190	*	*	*	*	*	*	*	*	*	*	*	*	*
136	-82	451	1009	395	-867	1932	-246	-1107	53	-213	-1507	-995	-790	-903	-1166	-221	-791	655	-1085	-927
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137	211	126	681	149	-889	-481	-268	-398	-52	-983	-1530	-1017	-56	-926	-1188	162	2257	308	-1108	-950
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	97
-	7	6304	9304	732	1329	3022	190	*	*	*	*	*	*	*	*	*	*	*	*	*
138	301	126	2141	341	421	17	759	-402	-415	148	-1530	-259	-812	-926	-3	-660	-826	-865	-1108	-950
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-	7	8304	9304	732	-1329	3022	-190	*	*	*	*	*	*	*	*	*	*	*	*	*
139	-647	126	-334	-188	-230	460	-268	-1488	-415	1560	-1530	-1017	676	-926	-179	-230	-826	-865	-1108	166
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-7	-8304	-9304	-732	-1329	-2386	-306	*	*	*	*	*	*	*	*	*	*	*	*	*
140	-706	67	-514	-384	-156	-540	700	-1547	-474	-480	310	-1076	-871	-985	82	2070	26	-924	771	-58
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-6	-8411	-9411	-732	-1329	-2916	-205	*	*	*	*	*	*	*	*	*	*	*	*	*
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143	-706	67	-190	-1264	-948	13	-327	-1547	1029	-76	207	-282	358	-985	-1247	-543	-712	-388	4036	-1008
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-	-6	-8411	-9411	-732	-1329	-2660	-248	*	*	*	*	*	*	*	*	*	*	*	*	*
144	-176	51	-1107	-1281	939	-556	-343	2019	-491	-488	303	-1093	-888	-1001	65	-307	-154	603	-1183	-1025
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-	-6	-8440	-9440	-732	-1329	-2839	-217	*	*	*	*	*	*	*	*	*	*	*	*	*
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-	-6	-8440	-9440	-732	-1329	-2839	-217	*	*											
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-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-94	-8440	-4051	-732	-1329	-2839	-217	*	*											
167	-675	99	-336	342	-917	-1675	603	-1516	392	-449	-1557	891	-840	-954	55	-935	134	-893	1026	-977
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-7	-8354	-9354	-732	-1329	-2937	-202	*	*											
168	-234	99	-772	468	-917	-509	1445	-1516	-443	-1011	-1557	2246	-840	-954	554	439	854	796	1149	977
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-	-100	-8354	-3965	-732	-1329	-2937	-202	*	*											
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-	-533	-8261	-1710	-732	-1329	-1974	-3106	*	*											
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-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-37	-9064	-5398	-732	-1329	-1801	-488	*	*											
177	-506	625	-1453	-1626	-1310	-902	451	-636	-315	-35	-1951	3086	-1234	-664	-612	-312	-1248	-350	-1529	-1371
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-42	-9030	-5215	-732	-1329	-1907	-448	*	*											
178	-478	-271	-729	217	-1286	-878	-665	-1885	214	-422	-1926	-1414	-1209	-529	-1585	2576	-547	-1262	1505	-1347
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	255	-97
-	-32	-8992	-5649	732	1329	-2015	410	*	*											

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179	-464	-253	-831	-731	-1268	-860	1667	-1967	-273	2152	-1909	207	-1192	-131	-174	-780	1206	-1244	-1467	-991
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-4	-8965	-9965	-732	-1329	-2087	-387	*	*	*	*	*	*	*	*	*	*	*	*	*
180	-1026	1326	-1411	2661	-497	-860	-647	-1867	-328	-378	-1909	-377	-534	-1305	-565	295	-1206	1244	-1487	-1329
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-45	-8965	-5112	-732	-1329	-2087	-387	*	*	*	*	*	*	*	*	*	*	*	*	*
181	-1000	-227	-1385	2820	-1242	-834	-621	-986	-768	-474	8	-68	-63	-1279	-530	-771	1180	-1218	-1461	-1303
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-46	-8924	-5082	-732	-1329	-2186	-358	*	*	*	*	*	*	*	*	*	*	*	*	*
182	-430	-201	-1358	-669	-420	-808	979	-1815	-742	-560	-259	-1344	-1139	3384	-496	-499	-1153	-1192	-1435	-1277
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-8	-8882	-8061	-732	-1329	-2277	-333	*	*	*	*	*	*	*	*	*	*	*	*	*
183	-972	593	-656	-253	-551	-805	-592	2968	-740	-1308	-1854	-1342	-1137	-1250	-171	-1231	-1151	-1190	1594	-1274
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-5	-8878	-9878	-732	-1329	-2285	-331	*	*	*	*	*	*	*	*	*	*	*	*	*
184	-972	-198	-191	494	-1213	-805	-592	-379	-740	2248	-1854	-1342	-1137	-1250	-1512	-716	-1151	-1190	-1432	-1274
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-5	-8878	-9878	-732	-1329	-2285	-331	*	*	*	*	*	*	*	*	*	*	*	*	*
185	-972	-198	-1356	2844	-1213	-805	196	-718	-158	-346	540	-1342	-1137	-1250	-620	-1231	-1151	-1190	-1432	-1274
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-5	-8878	-9878	-732	-1329	-2285	-331	*	*	*	*	*	*	*	*	*	*	*	*	*
186	-546	-198	-1356	-349	-1213	-269	-592	-447	-292	-747	-1854	-1342	-1137	-1250	-1022	2553	-181	-1190	-1432	-1274
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
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187	972	680	1356	667	1213	805	-592	-483	-375	-1308	4084	-1342	-1137	-1250	-620	76	-1151	-1190	512	-1274
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188	2515	198	551	1530	1213	805	592	996	-740	168	-444	-1342	-1137	-1250	-1512	134	-1151	-1190	-1432	-1274
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-5	-8878	-9878	-732	-1329	-2285	-331	*	*	*	*	*	*	*	*	*	*	*	*	*
189	-189	-198	-766	-53	-1213	-805	-592	-1813	-292	-754	53	-442	-1137	-1250	-1512	-414	-1151	-1190	4990	-1274
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-	-5	-8878	-9878	-732	-1329	-2285	-331	*	*	*	*	*	*	*	*	*	*	*	*	*
190	-420	108	-179	2768	-1213	-805	176	-1813	-375	-1308	-1854	-1342	-1137	-1250	-759	-800	-1151	-1190	1372	437
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-	-5	-8878	-9878	-732	-1329	-2285	-331	*	*	*	*	*	*	*	*	*	*	*	*	*
191	-972	-198	-1356	-976	-443	-805	-592	-1813	2851	135	-1854	171	-1137	-1250	-734	-716	-1151	-1190	850	-1274
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192	21	-179	-1337	-648	-1195	2677	-574	-1794	-721	-1289	-1835	-1323	-449	-1232	-217	313	-1132	-1171	-1414	-1255
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-	-137	-8848	-3495	-732	-1329	-2344	-316	*	*	*	*	*	*	*	*	*	*	*	*	*
193	-872	-99	-1257	-1430	-1114	-706	-493	-1713	-51	-346	-1755	-1242	-1038	-1151	-1413	2652	-1051	-1090	2215	-1175
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-	-52	-8714	-4927	-732	-1329	-2567	-267	*	*	*	*	*	*	*	*	*	*	*	*	*
194	-442	-71	-1229	-1403	-278	-134	-465	-1686	105	-1091	-1727	-1215	-1010	-833	-1055	2681	-869	-1063	-1305	-1147
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-5	-8668	-9668	-732	-1329	-2634	-253	*	*	*	*	*	*	*	*	*	*	*	*	*
195	-845	-71	-517	-1403	-1086	-678	-419	-1686	-613	2332	-1727	-996	-952	-1123	-631	122	-569	-1063	-1305	-1147
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196	-845	-71	-286	-1076	-1086	-678	-465	-1686	-269	-438	-130	-677	-164	41	-73	-335	-54	27	-12	255	.97
-	206	979	-178	-352	-36	372	585	-635	438	*	-620	-1727	3308	-1010	-1123	-1385	281	1024	1063	1305	-1147
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197	-845	-71	-1229	-1403	-1086	-678	-465	-829	-613	-438	-620	-1727	3308	-1010	-1123	-1385	281	1024	1063	1305	-1147
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	255	.97	
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198	-722	-71	-1229	-1403	-1086	-678	-465	-1686	-157	-438	-130	-677	-164	41	-73	-335	-54	27	-12	255	.97
-	206	979	-178	-352	-36	372	585	-635	438	*	-130	-677	-164	41	-73	-335	-54	27	-12	255	.97
-	-5	-8668	-9668	-732	-1329	-2634	-253	*	*	-613	-130	-677	-164	41	-73	-335	-54	27	-12	255	.97
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-	-1895	-8668	-457	-732	-1329	-2634	-253	*	*	201	-367	-913	-401	-196	-309	-571	713	-210	-249	2699	93
200	-31	743	-415	-589	127	136	349	-872	201	-438	-130	-677	-164	41	-73	-335	-54	27	-12	255	.97
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-	-20	-6747	-7747	-732	-1329	-3653	-119	*	*	-872	190	-913	-401	437	-309	-571	-290	-210	-249	491	333
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202	135	793	344	-539	-222	186	398	-822	273	-438	-130	-677	-164	41	-73	-335	-54	27	-12	255	.97
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-	-23	-6560	-7560	-732	-1329	-3688	-117	*	*	251	-199	-863	-351	-146	-259	267	-241	160	319	441	283
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-	-29	6236	7236	732	1329	3735	113	*	*	326	-242	-788	-276	-71	496	-447	321	-85	-104	366	208
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-	-29	-6236	-7236	-732	-1329	-3735	-113	*	*	326	-242	-788	-276	-71	496	-447	321	-85	-104	366	208
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-	206	979	-178	-352	-36	372	585	-635	438	*	-130	-677	-164	41	-73	-335	-54	27	-12	255	.97
-	-29	-6236	-7236	-732	-1329	-3735	-113	*	*	326	-242	-788	-276	-71	496	-447	321	-85	-104	366	208
207	210	868	-290	72	-148	260	473	-747	326	-438	-130	-677	-164	41	-73	-335	-54	27	-12	255	.97
-	206	979	-178	-352	-36	372	585	-635	438	*	-130	-677	-164	41	-73	-335	-54	27	-12	255	.97
-	-220	-6236	-2961	-732	-1329	-3735	-113	*	*	364	-204	-750	554	-33	-147	-409	-128	-47	-86	-329	171
208	132	905	-116	30	-110	298	511	-709	364	-438	-130	-677	-164	41	-73	-335	-54	27	-12	255	.97
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-	-59	-6047	-5326	-732	-1329	-3757	-111	*	*	385	-199	-745	-233	-28	-142	717	-123	-42	-81	-324	166
209	137	910	-247	-421	-105	303	516	-704	385	-438	-199	-745	-233	-28	-142	717	-123	-42	-81	-324	166
-	-	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
-	-	*	*	*	*	*	*	*	0	*	*	*	*	*	*	*	*	*	*	*	*

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13	206	979	-178	352	-36	372	585	-635	438	-130	577	-164	41	-73	-335	54	27	12	-255	97
	7	8240	-8240	-732	1329	3095	180	*	*											
	94	152	995	1170	508	446	-233	467	501	368	1494	982	777	-891	581	872	791	830	3489	-914
	206	979	178	352	-36	372	585	-635	438	-130	677	-164	41	-73	335	54	27	12	255	97
	7	-8240	-9240	-732	-1329	-3095	-180	*	*											
14	-612	162	100	-159	854	-446	-233	195	836	-20	-1494	-982	777	-891	-519	155	1546	-830	1563	261
	206	979	-178	-352	-36	372	585	-635	438	-130	-577	-164	41	-73	-335	-54	27	-12	-255	-97
	7	-8240	-9240	-732	-1329	-3095	-180	*	*											
15	-612	696	-996	-241	326	-446	-233	-162	295	1172	-1494	-982	-777	228	45	-369	422	135	-1073	-914
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	7	-8240	-9240	-732	-1329	-3095	-180	*	*											
16	-612	1559	-996	-505	1971	-446	988	-306	21	-304	-1494	225	-777	-891	-211	-50	104	-830	-1073	956
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	7	-8240	-9240	-732	-1329	-3095	-180	*	*											
17	22	162	100	-788	703	-446	1210	-1453	-380	924	-1494	-982	136	1877	-755	-872	-791	-830	-1073	-720
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	95	-8240	-4052	-732	-1329	-3095	-180	*	*											
18	318	1574	-952	843	-347	-401	2740	-1409	-336	-121	-1450	12	-80	-846	-1108	-827	-277	44	-1028	-870
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	8	-8152	-9152	-732	-1329	-2694	-242	*	*											
19	497	162	-301	484	394	-304	1087	-250	-380	-340	-1494	-982	-777	228	-1153	-872	1719	-830	-1073	-914
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	7	-8240	-9240	-732	-1329	-3095	-180	*	*											
20	-118	1485	-996	-241	-854	-377	233	-688	-380	1427	-1494	-982	-777	228	641	-578	160	-830	-167	-194
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	7	-8240	-9240	-732	-1329	-3095	-180	*	*											
21	612	1249	-996	-505	-854	-446	988	-250	-270	-22	-1494	-982	217	1877	649	-872	29	526	-1073	-914
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	94	-8240	-4063	-732	-1329	-3095	-180	*	*											
22	-568	206	100	-310	-810	-402	344	133	398	-904	-1450	1762	-80	-847	971	-828	73	98	-1028	-870
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	8	-8153	-9153	-732	-1329	-3161	-171	*	*											
23	-568	740	-952	1330	-810	-402	1205	-109	398	826	-1346	192	-733	-847	243	-828	-747	-786	-1028	-870
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	8	-8153	-9153	-732	-1329	-2697	-242	*	*											
24	-612	1559	-996	-1170	235	-446	-46	240	-380	55	646	-99	-403	793	-298	-745	-791	-830	1324	2161
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	7	-8240	-9240	-732	-1329	-3095	-180	*	*											
25	-612	2167	330	1286	235	-446	-233	-1453	418	-146	-1494	-982	279	-891	-1153	-745	199	-830	2074	-914
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	7	-8240	-9240	-732	-1329	-3095	-180	*	*											
26	-612	986	700	-192	-854	-446	-233	-1453	-380	1455	-1494	94	-777	-891	-1153	-248	476	32	-1073	-914
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	7	-8240	-9240	-732	-1329	-3095	-180	*	*											
27	-612	2265	996	574	311	-446	-233	-1453	-380	38	2600	-982	-777	-891	1017	-872	-321	-830	-1073	-914
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	7	-8240	-9240	-732	-1329	-3095	-180	*	*											
28	-371	162	430	-1047	819	-446	2074	-1335	-133	-704	740	-982	-777	938	1668	-562	-762	-29	-1073	-914
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	86	-8240	-4201	-732	-1329	-3095	-180	*	*											

29	572	201	1643	48	-814	406	1028	130	733	-240	1454	-942	65	-36	-232	-705	178	-790	-1033	-875
	206	979	-178	-352	-36	372	585	-635	438	-130	677	164	41	-73	-335	54	27	12	-255	97
	51	8161	-5004	-732	-1329	-3156	-172	*	*											
30	550	223	1134	392	436	-384	727	-1392	-319	-100	1433	-921	-716	-829	1674	-810	90	-337	-1011	853
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-63	8119	-4672	-732	-1329	-2769	-229	*	*											
31	-565	209	-171	-1123	-806	-398	2824	-1406	-333	235	-1447	-935	-730	1402	755	-3	-162	-783	-1025	-867
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-8	8149	-9149	-732	-1329	-2650	-250	*	*											
32	-612	1445	-996	-354	-854	-446	1160	92	-380	1440	-1494	-982	-746	617	-1153	-91	-791	213	-1073	-914
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-7	8240	-9240	-732	-1329	-3095	-180	*	*											
33	-612	162	1655	-927	-854	-446	852	419	-380	-277	-156	93	-777	-76	-1153	-311	-791	-29	-1073	946
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-7	8240	-9240	-732	-1329	-3095	-180	*	*											
34	612	511	347	353	-854	-119	424	-438	-380	132	-35	790	-777	2213	-1153	-872	-791	-830	-1073	-914
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	485	3240	-1826	-732	-1329	-1815	-482	*	*											
35	240	2643	-958	71	-815	-407	-194	1517	-341	-674	-1456	-943	-249	1029	-1114	-833	-752	70	-1034	444
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-8	8167	9167	-732	-1329	-2817	-221	*	*											
36	58	1399	-848	362	379	-433	-220	-1441	-212	-75	2431	-970	-765	-135	-507	-357	671	-818	1138	-902
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-7	8215	-9215	-732	-1329	-3111	-177	*	*											
37	-268	174	984	703	358	-433	-220	-1441	361	854	2431	-970	-716	-878	-1140	-859	385	818	1060	902
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	54	27	12	255	97
	-7	8215	-9215	-732	-1329	-3111	-177	*	*											
38	-599	3109	-984	-223	-841	-433	-220	-1441	-12	672	530	-970	-525	374	435	-859	779	818	1060	1161
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	54	27	-12	-255	97
	-7	8215	-9215	-732	-1329	-3111	-177	*	*											
39	370	1571	984	-913	120	157	98	484	-87	-936	1237	-970	-638	-655	496	1247	-779	-17	-1060	902
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-7	8215	-9215	-732	-1329	-3111	-177	*	*											
40	103	174	17	-1157	-379	-433	-220	-1183	128	-192	2983	-970	-765	485	-367	-681	-779	324	-1060	479
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-7	8215	-9215	-732	-1329	-3111	-177	*	*											
41	465	916	479	-109	406	-433	864	-26	-368	-936	-1482	160	-765	-878	-74	-859	-779	-818	-1060	2315
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-7	8215	-9215	-732	-1329	-3111	-177	*	*											
42	-599	174	-984	-1157	-841	1307	1001	-948	758	-936	-1482	-258	-765	374	451	-859	-62	-17	2111	597
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-7	8215	-9215	-732	-1329	-3111	-177	*	*											
43	-599	174	-984	-1157	301	-433	1676	1578	-368	39	-469	-970	-765	374	-1140	-455	143	702	-1060	-902
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-7	8215	-9215	-732	-1329	-3111	-177	*	*											
44	-370	3425	-17	-1157	-120	-433	-220	-1121	308	360	753	-970	-765	110	-1140	-859	687	-818	-1060	-902
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
	-7	8215	-9215	-732	-1329	-3111	-177	*	*											
45	103	174	479	-1157	720	-433	-220	-1441	1868	-831	-1482	-20	-765	1322	-1140	-859	150	-818	-1060	-902
	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97

46	7	-8215	9215	-732	-1329	3111	-177	*	373	*	380	165	1482	-970	765	1237	1140	839	779	1332	1060	903
	599	174	418	701	-841	433	220	373	-635	438	-130	577	-164	41	-73	335	54	27	1332	1060	903	
	206	979	-178	-352	-36	372	585	-635	-635	438	-130	577	-164	41	-73	335	54	27	1332	1060	903	
	-7	-8215	-9215	-732	-1329	3111	-177	*	-177	*	*	*	*	*	*	*	*	*	*	*	*	
47	-599	174	984	388	816	-433	665	-128	-128	1471	194	530	-970	-765	-878	-1140	-859	-449	66	-1060	688	
	206	979	-178	-352	-36	372	585	-635	-635	438	-130	-677	-164	41	-73	-335	54	27	66	-1060	688	
	-7	-8215	-9215	-732	-1329	3111	-177	*	-177	*	*	*	*	*	*	*	*	*	*	*	*	
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	206	979	-178	-352	-36	372	585	-635	-635	438	-130	-677	-164	41	-73	-335	-54	27	818	-1060	-902	
	-7	-8215	-9215	-732	-1329	3111	-177	*	-177	*	*	*	*	*	*	*	*	*	*	*	*	
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	206	979	-178	-352	-36	372	585	-635	-635	438	-130	-677	-164	41	-73	-335	54	27	818	-1060	-902	
	-7	-8215	-9215	-732	-1329	3111	-177	*	-177	*	*	*	*	*	*	*	*	*	*	*	*	
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	206	979	-178	-352	-36	372	585	-635	-635	438	-130	-677	-164	41	-73	-335	-54	27	-483	-1060	-902	
	-7	-8215	-9215	-732	-1329	3111	-177	*	-177	*	*	*	*	*	*	*	*	*	*	*	*	
51	90	174	-984	-84	-841	-433	1508	-1441	-1441	-368	843	530	-61	-765	973	618	-357	85	818	-1060	-902	
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	-7	-8215	-9215	-732	-1329	3111	-177	*	-177	*	*	*	*	*	*	*	*	*	*	*	*	
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	-7	-8215	-9215	-732	-1329	3111	-177	*	-177	*	*	*	*	*	*	*	*	*	*	*	*	
53	-599	174	106	-1157	1880	156	-220	-294	-294	-368	-292	-1482	-970	-96	-878	515	-766	791	818	-1060	1183	
	206	979	-178	-352	-36	372	585	-635	-635	438	-130	-677	-164	41	-73	-335	-54	27	818	-1060	1183	
	-7	-8215	-9215	-732	-1329	3111	-177	*	-177	*	*	*	*	*	*	*	*	*	*	*	*	
54	-599	174	-567	-213	999	-25	864	-295	-295	1471	128	659	-970	-765	594	-1140	-859	-779	50	-1060	-902	
	206	979	-178	-352	-36	372	585	-635	-635	438	-130	-677	-164	41	-73	-335	-54	27	50	-1060	-902	
	-7	-8215	-9215	-732	-1329	3111	-177	*	-177	*	*	*	*	*	*	*	*	*	*	*	*	
55	-599	1398	984	-776	672	-433	-220	1563	1563	-333	540	725	106	-765	402	-1140	-859	-779	818	-1060	-902	
	206	979	-178	-352	-36	372	585	-635	-635	438	-130	-677	-164	41	-73	-335	-54	27	818	-1060	-902	
	-7	-8215	-9215	-732	-1329	3111	-177	*	-177	*	*	*	*	*	*	*	*	*	*	*	*	
56	90	1074	133	-84	306	-433	-220	1641	1641	270	-936	888	751	-765	-878	-1140	-75	-779	818	-1060	-902	
	206	979	-178	-352	-36	372	585	-635	-635	438	-130	-677	-164	41	-73	-335	-54	27	818	-1060	-902	
	-7	-8215	-9215	-732	-1329	3111	-177	*	-177	*	*	*	*	*	*	*	*	*	*	*	*	
57	-599	174	-984	-1157	-841	-433	-220	-129	-129	876	-240	756	-258	-765	110	225	-859	-779	1474	-1060	1161	
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	-7	-8215	-9215	-732	-1329	3111	-177	*	-177	*	*	*	*	*	*	*	*	*	*	*	*	
58	-599	1541	497	-1157	-841	-433	1060	-426	-426	833	-936	753	-970	-765	-878	376	-859	1405	367	-1060	-902	
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	-7	-8215	-9215	-732	-1329	3111	-177	*	-177	*	*	*	*	*	*	*	*	*	*	*	*	
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	-7	-8215	-9215	-732	-1329	3111	-177	*	-177	*	*	*	*	*	*	*	*	*	*	*	*	
60	-599	174	34	-228	-841	-433	1586	-295	-295	366	-240	924	-190	-765	332	-1140	-23	-779	818	-1060	2174	
	206	979	-178	-352	-36	372	585	-635	-635	438	-130	-677	-164	41	-73	-335	-54	27	818	-1060	2174	
	-7	-8215	-9215	-732	-1329	3111	-177	*	-177	*	*	*	*	*	*	*	*	*	*	*	*	
61	-300	963	-315	-402	-1141	-733	308	1827	1827	1169	-225	-1781	-1269	-69	-4	-985	-1159	-1078	-582	-1360	999	
	206	979	-178	-352	-36	372	585	-635	-635	438	-130	-677	-164	41	-73	-335	-54	27	-582	-1360	999	
	-5	-8756	-9756	-732	-1329	-2548	-271	*	-1740	-667	-173	3033	-810	-1064	882	-215	-534	-1078	-1117	-1360	-1201	
62	-899	-125	1890	-1457	-1141	-57	-520	-1740	-1740	-667	-173	3033	-810	-1064	882	-215	-534	-1078	-1117	-1360	-1201	

206	979	178	352	36	372	585	-635	438	-130	577	-164	41	-73	335	54	27	-12	-255	97
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63	241	1101	1283	1457	1141	733	-536	-28	790	3158	-34	-1064	693	235	1159	-1078	-255	-1360	1201
206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	73	335	-54	27	12	-255	97
-5	-8756	9756	-732	-1329	2548	-271	*	*											
64	214	3570	1457	52	733	-520	-219	-28	-261	-1781	38	1364	103	-665	-337	-1078	-1117	-1360	-25
-	206	979	-178	-352	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-5	-8756	9756	-732	1329	2548	-271	*	*											
65	-899	1159	1283	1457	479	-221	-1416	480	-256	-532	-1269	504	-697	-1440	1743	-1078	-1117	-1360	-1201
206	979	-178	-352	36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-5	-8756	9756	-732	-1329	-2548	-271	*	*											
66	928	1559	-1283	-527	-1141	733	801	-45	-696	3191	-1269	-1064	758	-1440	-1159	-1078	-255	-1360	-1201
-	206	979	-178	-352	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-5	-8756	9756	-732	-1329	-2548	-271	*	*											
67	-196	2696	1283	1457	-1141	-733	-520	-593	-591	-1781	161	-1064	-1178	-1440	-1159	-496	1386	-1360	2644
-	206	979	-178	-352	-36	372	585	-635	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-5	-8756	9756	-732	-1329	-2548	-271	*	*											
68	314	620	1283	1457	-51	1731	-520	-46	-851	-1781	-34	-1064	1784	-1440	-565	-1078	-358	-1360	899
-	206	979	-178	-352	-36	372	585	-635	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-5	-8756	9756	-732	-1329	-2548	-271	*	*											
69	-899	-125	1283	915	-653	-107	17	1915	-539	803	-1269	-1064	-1178	-282	123	-258	135	-1360	-298
206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-257	-8756	-2636	-732	-1329	-1152	-862	*	*											
70	-320	3550	-1303	-428	-510	381	-854	-1760	-132	-1255	-1801	-1084	-1197	-255	300	1236	-154	-1379	431
-	206	979	-178	-352	-36	372	585	-635	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-5	-8789	-9789	-732	-1329	-2498	-281	*	*											
71	7	1230	1303	-1477	1636	-470	540	-223	-559	-1801	-338	-1084	-1197	-1460	-1179	-1098	735	1379	365
-	206	979	-178	-352	-36	372	585	-635	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-5	-8789	-9789	-732	-1329	-2498	-281	*	*											
72	541	-145	-1303	-1477	-1161	-753	-540	-86	-586	-65	-1289	-1084	-1197	-1005	-1179	-169	1708	-1379	1665
-	206	979	-178	-352	-36	372	585	-635	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-5	-8789	9789	-732	-1329	-2498	-281	*	*											
73	-439	542	162	-1477	60	-753	-540	-457	-586	-459	-1289	-1084	-1197	1777	-894	-1098	-336	-1379	-1221
-	206	979	-178	-352	-36	372	585	-635	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-5	-8789	-9789	-732	-1329	-2498	-281	*	*											
74	-919	1139	-1303	-810	-1161	-162	-540	-1760	-279	-1801	2157	-1084	-1197	-125	-342	-163	1267	-1379	-1221
-	206	979	-178	-352	-36	372	585	-635	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-5	-8789	-9789	-732	-1329	-2498	-281	*	*											
75	-814	685	-1303	-428	-1161	-753	-540	1879	-132	846	-1801	-1289	-170	-1460	65	-1098	315	-1379	-1221
-	206	979	-178	-352	-36	372	585	-635	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-5	-8789	-9789	-732	-1329	-2498	-281	*	*											
76	-919	-145	1951	-465	-198	-753	682	1385	-3	-1801	-647	310	-448	-1460	-461	-431	-1137	-1379	-1221
-	206	979	-178	-352	-36	372	585	-635	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-5	-8789	-9789	-732	-1329	-2498	-281	*	*											
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-5	-8789	-9789	-732	-1329	-2498	-281	*	*											
78	-229	-145	-1303	1368	-1161	-753	683	-470	-610	-1801	-82	-1084	-1197	-302	-553	-516	-316	-1379	-1221
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92	232	149	-1008	-366	1934	-458	-245	-1465	-392	-664	-1506	-355	-789	1139	656	-68	-803	41	-1085	657
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93	-26	1433	-42	-1182	-866	-458	-245	-1465	-392	-960	2588	-994	553	-159	40	-68	6	164	-1085	998
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PCT/US00/10302

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-	-1	-10578	-11578	-732	-1329	-2637	-253	*	*	*	*	*	*	*	*	*	*	*	*	*	*
16	-592	-1512	1475	-1458	1056	-2120	754	-818	*	712	-283	446	-2656	1396	-2565	-301	-1444	842	-269	-2746	-348
-	206	979	-178	-352	-36	372	585	-635	*	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-1	-10636	-11636	-732	-1329	-3706	-115	*	*	*	*	*	*	*	*	*	*	*	*	*	*
17	408	-1512	420	-1153	-939	767	764	608	*	-599	418	2180	-2656	-774	-507	94	-565	-784	-1001	-2746	-390
-	206	979	-178	-352	-36	372	585	-635	*	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-1	-10636	-11636	-732	-1329	-3706	-115	*	*	*	*	*	*	*	*	*	*	*	*	*	*
18	-83	-1512	-674	-902	142	-2120	-388	932	*	146	-421	2322	317	1232	-1444	-1168	-1364	-366	718	-2746	-460
-	206	979	-178	-352	-36	372	585	-635	*	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-1	-10636	-11636	-732	-1329	-3706	-115	*	*	*	*	*	*	*	*	*	*	*	*	*	*
19	-1030	-1512	1215	377	465	-853	313	207	*	172	-1336	-1234	-337	-76	1488	1103	-874	-47	-1242	-2746	-755
-	206	979	-178	-352	-36	372	585	-635	*	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-1	-10636	-11636	-732	-1329	-3706	-115	*	*	*	*	*	*	*	*	*	*	*	*	*	*
20	-1239	-24	-681	1522	-853	-2120	202	-1226	*	1466	307	-3168	-335	382	-785	766	-1336	-2465	-1242	-2746	1427
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-	-1	-10636	-11636	-732	-1329	-3706	-115	*	*	*	*	*	*	*	*	*	*	*	*	*	*
21	604	-1512	-273	199	1041	-914	1249	-1089	*	-130	228	-1661	1954	590	-282	-1227	-1344	-731	-2023	-2746	-2588
-	206	979	-178	-352	-36	372	585	-635	*	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-1	-10636	-11636	-732	-1329	-2966	-198	*	*	*	*	*	*	*	*	*	*	*	*	*	*
22	-2250	-1537	862	-1156	1594	-344	812	-2628	*	-212	1368	69	-652	104	-1131	798	-2570	225	-2035	-2771	-429
-	206	979	-178	-352	-36	372	585	-635	*	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-88	-10664	-4089	-732	-1329	-3629	-122	*	*	*	*	*	*	*	*	*	*	*	*	*	*
23	-716	-1463	784	191	2078	-146	-1857	-2001	*	251	1062	-3118	-2606	-1208	-485	-149	-588	572	-1986	-2697	-2538
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-	-37	-10577	-5337	-732	-1329	-3836	-105	*	*	*	*	*	*	*	*	*	*	*	*	*	*
24	-1845	327	1626	-788	915	-272	728	-757	*	80	-488	-2576	-125	-693	-2066	741	-1782	1301	-40	-2666	-442
-	206	979	-178	-352	-36	372	585	-635	*	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-35	-10541	-5436	-732	-1329	-3914	-99	*	*	*	*	*	*	*	*	*	*	*	*	*	*
25	-2178	-1405	697	236	1989	-750	-913	27	*	-81	-891	-3060	-1030	277	234	418	-302	-2357	815	-1962	593
-	206	979	-178	-352	-36	372	585	-635	*	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-14	-10507	-6811	-732	-1329	-2264	-337	*	*	*	*	*	*	*	*	*	*	*	*	*	*

26	-699	630	-642	-115	727	-948	1109	-3098	864	370	849	-1398	1026	-252	301	-556	-502	-679	-2718	864
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-40	-10602	-5226	-732	-1329	-3439	-140	*	*											
27	-700	-1461	227	1426	-299	-1272	551	-458	1442	-2234	-3021	-1283	1052	-2513	57	-408	29	-357	-2695	575
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-37	-10575	-5353	-732	-1329	-1781	-496	*	*											
28	-892	-1551	829	-1786	1667	-478	2447	-862	172	-702	-3207	181	657	-1619	734	-310	-335	-881	-1249	-1818
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-88	-10681	-4088	-732	-1329	-2756	-231	*	*											
29	-1497	55	-917	780	882	-954	1004	-1257	499	596	-3161	-2649	-966	-687	1631	-505	-72	-949	-457	523
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-61	-10628	-4613	-732	-1329	-1791	-492	*	*											
30	-2085	-1560	1339	-774	2034	104	1102	-339	-376	-2090	-231	-2704	-887	-482	265	-1212	457	-653	-2794	1724
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-44	-10692	-5087	-732	-1329	-3158	-171	*	*											
31	-1407	-1535	488	1228	752	-1133	-881	-3150	-1810	14	-3191	-2679	8	889	420	386	493	541	-2769	267
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-32	-10662	-5531	-732	-1329	-1976	-423	*	*											
32	-1206	737	-245	426	-2602	873	1673	295	338	-2170	-3242	-860	-2525	-418	1166	-46	781	-338	-2820	153
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-201	-10723	-2950	-732	-1329	-1997	-416	*	*											
33	451	-1007	-985	302	-774	-946	117	235	205	-2593	-3139	-2627	371	-2536	1181	627	1074	130	-2718	494
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-110	-10601	-3778	-732	-1329	-892	-1117	*	*											
34	-1996	68	-377	-969	-830	-188	1427	791	-25	-2742	102	-2776	120	996	-321	76	1047	1202	-2867	-572
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-30	-10777	-5624	-732	-1329	-1810	-484	*	*											
35	-698	-1667	-2825	-1534	-2683	-2275	482	52	-104	-2777	918	-2811	1688	-2720	601	1428	1104	-249	-2901	1130
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-	-209	-10817	-2895	-732	-1329	-2579	-264	*	*											
36	-2279	1479	-193	379	-2521	492	865	-967	-546	-2227	-3162	-2649	100	422	386	-71	1339	82	-2740	1719
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-126	-10628	-3596	-732	-1329	-1304	-749	*	*											
37	-2340	-1567	-729	-2898	-655	-2174	-265	794	-351	-720	-3222	-1051	435	-2619	1477	-292	2256	-1399	-2801	1236
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-1	-10700	-11700	-732	-1329	-2054	-398	*	*											
38	-554	-1629	-352	130	-758	-1248	-139	-982	774	-83	-251	-85	-76	-2681	793	-826	1955	-423	-2863	-577
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-	-1	-10773	-11773	-732	-1329	-3308	-154	*	*											
39	-1687	-1629	-361	-378	-822	-1310	-2024	-581	740	213	-3285	-2773	453	-539	2542	-190	-269	-634	-2863	-696
-	206	979	-178	-352	-36	372	585	-635	438	-130	-677	-164	41	-73	-335	-54	27	-12	-255	-97
-	-1	-10773	-11773	-732	-1329	-1861	-465	*	*											
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-	-85	-10839	-4147	-732	-1329	-2049	-399	*	*											
41	38	-1647	111	962	-2662	-685	27	-3261	-524	-1980	-2224	-632	1497	-1459	35	-584	955	853	-2881	1205